			factors, and hormones are well	described below under
			known in the art and may be	"Infectious Disease"). Highly
		7	used or routinely modified to	preferred indications include
	_		assess the ability of	autoimmune diseases (e.g.,
	-	-	polypeptides of the invention	rheumatoid arthritis, systemic
			(including antibodies and	lupus erythematosis, multiple
			agonists or antagonists of the	sclerosis and/or as described
	_	-	invention) to mediate	below) and
			immunomodulation and	immunodeficiencies (e.g., as
			differentiation and modulate T	described below). Highly
			cell proliferation and function.	preferred indications also
			Exemplary assays that test for	include boosting a B cell-
	_	• • •	immunomodulatory proteins	mediated immune response
			evaluate the production of	and alternatively suppressing a
	•		cytokines, such as IL-6, and	B cell-mediated immune
-			the stimulation and	response. Highly preferred
			upregulation of T cell	indications include
		1	proliferation and functional	inflammation and
			activities. Such assays that	inflammatory
			may be used or routinely	disorders.Additional highly
	****	1	modified to test	preferred indications include
			immunomodulatory and	asthma and allergy. Highly
			diffferentiation activity of	preferred indications include
			polypeptides of the invention	neoplastic diseases (e.g.,
	•	<u> </u>	(including antibodies and	myeloma, plasmacytoma,
			agonists or antagonists of the	leukemia, lymphoma,
		<u> </u>	invention) include assays	melanoma, and/or as described
			disclosed in Miraglia et al., J	below under
			Biomolecular Screening 4:193-	"Hyperproliferative
			204(1999); Rowland et al.,	Disorders"). Highly preferred
		-	"Lymphocytes: a practical	indications include neoplasms

			annroach" Chanter 6:138-160	and cancers such as myeloma
			(A) OOO Tarabase of the test o	als and carried bearing and
-			(2000); and vernasselt et al., J	piasmacytoma, leukemia,
			Immunol 158:2919-2925	lymphoma, melanoma, and
			(1997), the contents of each of	prostate, breast, lung, colon,
			which are herein incorporated	pancreatic, esophageal,
			by reference in its entirety.	stomach, brain, liver and
			Human dendritic cells that may	urinary cancer. Other preferred
	_		be used according to these	indications include benign
			assays may be isolated using	dysproliferative disorders and
			techniques disclosed herein or	pre-neoplastic conditions, such
			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
			antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
	~		upregulate T cell proliferation	lymphocytic anemia (ALL),
	,—		and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
		-		reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
				diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an

					infectious disease as described below under "Infectious Disease").
228	HHEPD24	1176	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
				effects on B cells. IL-6	embodiment of the invention includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
	· ·			IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
		-		IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
		· ·		has been linked to autoimmune	highly preferrred indication is
		-		disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
				immunomodulation and	immunodeficiencies (e.g., as

	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
-	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and

				techniques disclosed herein or	pre-neoplastic conditions, such
	-			otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
			•		granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additional preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HHEPD24	1176	Production of	MCP-1 FMAT. Assays for	A highly preferred
228			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred

		cells are well known in the art	embodiment of the invention
		and may be used or routinely	includes a method for
-		modified to assess the ability	inhibiting (e.g., reducing)
		of polypeptides of the	MCP-1 production. A highly
		invention (including antibodies	preferred indication is
		and agonists or antagonists of	infection (e.g., an infectious
		the invention) to mediate	disease as described below
		immunomodulation, induce	under "Infectious Disease").
		chemotaxis, and modulate	Additional highly preferred
		immune cell activation.	indications include
		Exemplary assays that test for	inflammation and
		immunomodulatory proteins	inflammatory disorders.
		evaluate the production of cell	Preferred indications include
		surface markers, such as	blood disorders (e.g., as
		monocyte chemoattractant	described below under
	-	protein (MCP), and the	"Immune Activity", "Blood-
		activation of monocytes and T	Related Disorders", and/or
		cells. Such assays that may be	"Cardiovascular Disorders").
		used or routinely modified to	Highly preferred indications
		test immunomodulatory and	include autoimmune diseases
		diffferentiation activity of	(e.g., rheumatoid arthritis,
		polypeptides of the invention	systemic lupus erythematosis,
		(including antibodies and	multiple sclerosis and/or as
	19	agonists or antagonists of the	described below) and
		invention) include assays	immunodeficiencies (e.g., as
		disclosed in Miraglia et al., J	described below). Preferred
		Biomolecular Screening 4:193-	indications also include
		204(1999); Rowland et al.,	anemia, pancytopenia,
		"Lymphocytes: a practical	leukopenia, thrombocytopenia,
		approach" Chapter 6:138-160	Hodgkin's disease, acute
		(2000); Satthaporn and	lymphocytic anemia (ALL),

					metaplasia, and/or dysplasia.
	HHEPD24	1176	Production of	MIP-1alpha FMAT. Assays	A highly preferred
228		`	MIP1alpha	for immunomodulatory	embodiment of the invention
				proteins produced by activated	includes a method for
				dendritic cells that upregulate	stimulating MIP1a production.
······				monocyte/macrophage and T	An alternative highly preferred
				cell chemotaxis are well	embodiment of the invention
				known in the art and may be	includes a method for
				used or routinely modified to	inhibiting (e.g., reducing)
				assess the ability of	MIP1a production. A highly
				polypeptides of the invention	preferred indication is
				(including antibodies and	infection (e.g., an infectious
_			-	agonists or antagonists of the	disease as described below
-				invention) to mediate	under "Infectious Disease").
				immunomodulation, modulate	Preferred indications include
				chemotaxis, and modulate T	blood disorders (e.g., as
				cell differentiation. Exemplary	described below under
				assays that test for	"Immune Activity", "Blood-
	-			immunomodulatory proteins	Related Disorders", and/or
				evaluate the production of	"Cardiovascular Disorders").
				chemokines, such as	Highly preferred indications
				macrophage inflammatory	include autoimmune diseases
				protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
				the activation of	systemic lupus erythematosis,
				monocytes/macrophages and T	multiple sclerosis and/or as
		-		cells. Such assays that may be	described below) and
				used or routinely modified to	immunodeficiencies (e.g., as
		•		test immunomodulatory and	described below). Additional
				chemotaxis activity of	highly preferred indications
				polypeptides of the invention	include inflammation and
				(including antibodies and	inflammatory disorders.

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Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,	asthma, and allergy.	Preferred indications also	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include
agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); Satthaporn and	Eremin, J R Coll Surg Ednb	45(1):9-19 (2001); Drakes et	al., Transp Immunol 8(1):17-	29 (2000); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.	
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benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated
	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate imflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or
	Production of TNF alpha by dendritic cells
	1176
	HHEPD24
	228

				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and upregulate T cell proliferation	leukopenia, thrombocytopenia, Hodgkin's disease, acute
-				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
			١		arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	-				cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
			797		under "Infectious Disease").
229	HHEPM33	1177	SEAP in 293/ISRE		
	HHEPM33	1177	Activation of	Assays for the activation of	A highly preferred indication
229			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
			response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred

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indication is diabetes mellitus.	An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as
(including antibodies and	agonists or antagonists of the	invention) to increase cAMP,	regulate CREB transcription	factors, and modulate	expression of genes involved	in a wide variety of cell	functions. For example, a	3T3-L1/CRE reporter assay	may be used to identify factors	that activate the cAMP	signaling pathway. CREB	plays a major role in	adipogenesis, and is involved	in differentiation into	adipocytes. CRE contains the	binding sequence for the	transcription factor CREB	(CRE binding protein).	Exemplary assays for	transcription through the	cAMP response element that	may be used or routinely	modified to test cAMP-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
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										-									•											

				Malm, Methods in Enzymol	described in the "Endocrine
				216:362-368 (1992); Henthorn	Disorders" section below),
				et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
		_		85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
-				et al., Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
				Klemm et al., J Biol Chem	(e.g., infectious diseases and
•				273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
				according to these assays are	Dupuytren's contracture).
				publicly available (e.g.,	Additional highly preferred
			****	through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
				Exemplary mouse adipocyte	resistance.
				cells that may be used	
				according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	
				fibroblast cells developed	
•				through clonal isolation and	
				undergo a pre-adipocyte to	
				adipose-like conversion under	
				appropriate differentiation	
				conditions known in the art.	
229	HHEPM33	1177	Activation of transcription	This reporter assay measures activation of the GATA-3	Highly preferred indications
			dansembasin	מכנו אמווסוו סו מוס סו זינים	moture and gy, asuma, and

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rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred
signaling pathway in HMC-1	human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate GATA3 transcription	factors and modulate	expression of mast cell genes	important for immune response	development. Exemplary	assays for transcription	through the GATA3 response	element that may be used or	routinely modified to test	GATA3-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and
through GATA-3	response element in	immune cells (such	as mast cells).								•																			
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				Malm Methods in Enzymol	indications include henion
				716.367-368 (1992): Henthorn	dysproliferative disorders and
				210.302-308 (1732), Hendidil	dyspionicianive disonders and
				et al., Froc Natl Acad Sci USA	pre-neoplastic conditions, such
				85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
				et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
				Quant Biol 64:563-571 (1999);	Preferred indications include
				Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
				J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
				(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
				Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
				Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
	•			immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HHEPM33	1177	Activation of	This reporter assay measures	Highly preferred indications
229			transcription	activation of the NFAT	include allergy, asthma, and

rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, melanoma,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary tract cancers and/or as	described below under	"Hyperproliferative	Disorders"). Other preferred
signaling pathway in HMC-1	numan mast cell line.	Activation of NFA1 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the Nuclear Factor of	Activated T cells (NFAT)	response element are well-	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFAT	transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays
through NFAT	response element in	ımmune cells (such	as mast cells).																											
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disclosed in Berger et al., Gene	indications include benign
66:1-10 (1998); Cullen and	dysproliferative disorders and
Malm, Methods in Enzymol	pre-neoplastic conditions, such
216:362-368 (1992); Henthorn	as, for example, hyperplasia,
et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
85:6342-6346 (1988); De Boer	
et al., Int J Biochem Cell Biol	
31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
et al., J Immunol	leukemias, Hodgkin's disease,
165(12):7215-7223 (2000);	acute lymphocytic anemia
Hutchinson and McCloskey, J	(ALL), plasmacytomas,
Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
 al., J Exp Med 188:527-537	granulomatous disease,
(1998), the contents of each of	inflammatory bowel disease,
which are herein incorporated	sepsis, neutropenia,
by reference in its entirety.	neutrophilia, psoriasis,
Mast cells that may be used	suppression of immune
 according to these assays are	reactions to transplanted
publicly available (e.g.,	organs and tissues, hemophilia,
through the ATCC).	hypercoagulation, diabetes
Exemplary human mast cells	mellitus, endocarditis,
that may be used according to	meningitis, and Lyme Disease.
these assays include the HMC-	
1 cell line, which is an	
immature human mast cell line	
established from the peripheral	
blood of a patient with mast	
cell leukemia, and exhibits	
many characteristics of	
immature mast cells.	

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Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Additional highly	preferred indications include	inflammation and	inflammatory disorders. An	additional highly preferred	indication is infection (e.g., an	infectious disease as described	below under "Infectious	Disease"). Preferred	indications include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative
Hig	includ	as des	"Imm	Relate	"Card	High	includ	(e.g.,	systen	multip	descri	immn	descri	cell-n	respoi	cell-m	respor	prefer	inflan	inflan	additi	indica	infect	below	Disea	indica	diseas	lympl	below	anH,,
Assays for the activation of	transcription through the	Nuclear Factor of Activated T	cells (NFAT) response element	are well-known in the art and	may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to regulate	NFAT transcription factors and	modulate expression of genes	involved in	immunomodulatory functions.	Exemplary assays for	transcription through the	NFAT response element that	may be used or routinely	modified to test NFAT-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85.6342-6346 (1988).
Activation of	transcription	through NFAT	response element in	immune cells (such	as natural killer	cells).																								
1177																														-
ННЕРМ33																														
	229		•																											

Disorders"), Preferred	indications include neoplasms	l and cancers, such as, for); example, leukemia, lymphoma,	and prostate, breast, lung,	colon, pancreatic, esophageal,	stomach, brain, liver and		indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	n plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	acthma and allerow
Aramburu et al., J Exp Med	182(3):801-810 (1995); De	Boer et al., Int J Biochem Cell	Biol 31(10):1221-1236 (1999);	Fraser et al., Eur J Immunol	29(3):838-844 (1999); and	Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which	are herein incorporated by	reference in its entirety. NK	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human NK cells	that may be used according to	these assays include the NK-	YT cell line, which is a human	natural killer cell line with	cytolytic and cytotoxic	activity.									
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	ННЕРМ33	1177	Activation of	Assays for the activation of	A preferred embodiment of
229			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
	<i>-</i> -			in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
		-		disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
	•			Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional
	4	4.		et al., Proc Natl Acad Sci USA	highly preferred indications
				85:6342-6346 (1988); Benson	include inflammation and
				et al., J Immunol 153(9):3862-	inflammatory disorders, and

treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),
3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.																
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					plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below
229	ННЕРМ33	1177	SEAP in NK16/STAT6		under "Infectious Disease").
229	ННЕРМ33	1177	Hexosaminidase in RBL-2H3		
229	HHEPM33	1177	Activation of transcription	Assays for the activation of	Highly preferred indications
			through GAS response element in	Gamma Interferon Activation Site (GAS) response element	(e.g., leukemia, lymphoma, and/or as described below
	18.00		immune cells (such as T-cells).	are well-known in the art and may be used or routinely	under "Hyperproliferative Disorders"), Highly preferred
				modified to assess the ability of polypeptides of the invention (including antibodies	indications include neoplasms and cancers, such as, for
				IIIVCIIIIVIII (IIIVIIUUIIII) AIIII VUUICS	example, leukemia, lymphoma

	and agonists or antagonists of	(e.g., T cell lymphoma,
-	the invention) to regulate	Burkitt's lymphoma, non-
	STAT transcription factors and	Hodgkins lymphoma,
	modulate gene expression	Hodgkin"s disease),
	involved in a wide variety of	melanoma, and prostate,
	cell functions. Exemplary	breast, lung, colon, pancreatic,
	assays for transcription	esophageal, stomach, brain,
-	through the GAS response	liver and urinary cancer. Other
	element that may be used or	preferred indications include
	routinely modified to test	benign dysproliferative
	GAS-response element activity	disorders and pre-neoplastic
	of polypeptides of the	conditions, such as, for
	invention (including antibodies	example, hyperplasia,
	and agonists or antagonists of	metaplasia, and/or dysplasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	contents of each of which are	preferred indications include
	herein incorporated by	inflammation and
	reference in its entirety.	inflammatory disorders.
		Highly preferred indications
		include blood disorders (e.g.,
7/100	may be used according to these	as described below under

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Highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers such as for
Assays for the activation of	transcription through the	NFKB response element are	well-known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Valle	Blazquez et al, Immunology	90(3):455-460 (1997)
Activation of	transcription	through NFKB	response element in	immune cells (such	as natural killer	cells).														-										
1178																											-			
HHEPT60																														
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				Aramburan et al. J Exp Med	example, melanoma, renal cell
				82(3):801-810 (1995): and	carcinoma, leukemia.
				Fraser et al., 29(3):838-844	lymphoma, and prostate,
				(1999), the contents of each of	breast, lung, colon, pancreatic,
				which are herein incorporated	esophageal, stomach, brain,
				by reference in its entirety.	liver and urinary cancer. Other
				NK cells that may be used	preferred indications include
				according to these assays are	benign dysproliferative
				publicly available (e.g.,	disorders and pre-neoplastic
	-			through the ATCC).	conditions, such as, for
				Exemplary human NK cells	example, hyperplasia,
				that may be used according to	metaplasia, and/or dysplasia.
				these assays include the NKL	Preferred indications also
				cell line, which is a human	include anemia, pancytopenia,
				natural killer cell line	leukopenia, thrombocytopenia,
				established from the peripheral	Hodgkin's disease, acute
				blood of a patient with large	lymphocytic anemia (ALL),
				granular lymphocytic	plasmacytomas, multiple
				leukemia. This IL-2 dependent	myeloma, Burkitt's lymphoma,
				suspension culture cell line has	arthritis, AIDS, granulomatous
				a morphology resembling that	disease, inflammatory bowel
				of activated NK cells.	disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
			•		reactions to transplanted
			,		organs, asthma and allergy.
	HHEPU04	6211	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
231				by T cells and has strong	embodiment of the invention

participates in IL-4 induced	stimulating (e.g., increasing)
IgE production and increases	IL-6 production. An alternative
IgA production (IgA plays a	highly preferred embodiment
role in mucosal immunity).	of the invention includes a
IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
Deregulated expression of IL-6	reducing) IL-6 production. A
has been linked to autoimmune	highly preferrred indication is
disease, plasmacytomas,	the stimulation or enhancement
myelomas, and chronic	of mucosal immunity. Highly
hyperproliferative diseases.	preferred indications include
Assays for immunomodulatory	blood disorders (e.g., as
and differentiation factor	described below under
proteins produced by a large	"Immune Activity", "Blood-
variety of cells where the	Related Disorders", and/or
expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
factors, and hormones are well	described below under
known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
· ·	IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation and differentiation and modulate T cell proliferation and function. Exemplary assays that test for immunomodulatory proteins evaluate the production of

cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory
may be used or routinely	disorders. Additional highly
modified to test	preferred indications include
immunomodulatory and	asthma and allergy. Highly
diffferentiation activity of	preferred indications include
polypeptides of the invention	neoplastic diseases (e.g.,
(including antibodies and	myeloma, plasmacytoma,
agonists or antagonists of the	leukemia, lymphoma,
invention) include assays	melanoma, and/or as described
disclosed in Miraglia et al., J	below under
Biomolecular Screening 4:193-	
204(1999); Rowland et al.,	Disorders"). Highly preferred
"Lymphocytes: a practical	indications include neoplasms
approach" Chapter 6:138-160	and cancers, such as, myeloma,
(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
Immunol 158:2919-2925	lymphoma, melanoma, and
(1997), the contents of each of	prostate, breast, lung, colon,
which are herein incorporated	pancreatic, esophageal,
by reference in its entirety.	stomach, brain, liver and
Human dendritic cells that may	-
be used according to these	indications include benign
assays may be isolated using	dysproliferative disorders and
techniques disclosed herein or	pre-neoplastic conditions, such
otherwise known in the art.	as, for example, hyperplasia,
Human dendritic cells are	metaplasia, and/or dysplasia.
antigen presenting cells in	Preferred indications include
 suspension culture, which,	anemia, pancytopenia,

				when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS,
					inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues,
					hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
231	HHEPU04	1179	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications

	the ability of polypeptides of	include blood disorders (e.g.,
	antibodies and agonists or	"Immune Activity", "Blood-
	antagonists of the invention) to	Related Disorders", and/or
	mediate immunomodulation,	"Cardiovascular Disorders"),
	modulate inflammation and	Highly preferred indications
	cytotoxicity. Exemplary	include autoimmune diseases
	assays that test for	(e.g., rheumatoid arthritis,
	immunomodulatory proteins	systemic lupus erythematosis,
	evaluate the production of	Crohn"s disease, multiple
	cytokines such as tumor	sclerosis and/or as described
	necrosis factor alpha (TNFa),	below), immunodeficiencies
	and the induction or inhibition	(e.g., as described below),
,	of an inflammatory or	boosting a T cell-mediated
	cytotoxic response. Such	immune response, and
	assays that may be used or	suppressing a T cell-mediated
	routinely modified to test	immune response. Additional
	immunomodulatory activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders, and
	agonists or antagonists of the	treating joint damage in
	invention) include assays	patients with rheumatoid
	disclosed in Miraglia et al., J	arthritis. An additional highly
	Biomolecular Screening 4:193-	preferred indication is sepsis.
	204(1999); Rowland et al.,	Highly preferred indications
	"Lymphocytes: a practical	include neoplastic diseases
	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
	(1198); Dahlen et al., J	Disorders"). Additionally,
	Immunol 160(7):3585-3593	highly preferred indications

include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma	tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other	preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia,	Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune	reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
(1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J	(1999), the contents of each of which are herein incorporated by reference in its entirety.	be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art.	Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen	and/or cytokines, initiate and upregulate T cell proliferation and functional activities.		

232	HHFBY53	1180	Activation of Endothelial Cell	Kinase assay. JNK and p38 kinase assays for signal	cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). A highly preferred embodiment of the invention
			p38 or JNK Signaling Pathway.	transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the	includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting embodiment of the invention includes a method for stimulating apoptosis of endothelial cells. An
				assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Gupta et al., Exp	alternative highly preferred embodiment of the invention includes a method for

inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating (e.g., increasing) endothelial cell activation. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) the	activation of analyor inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for	highly preferred embodiment of the invention includes a method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as
Cell Res 247(2): 495-504 (1999); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be	used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line	venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.

described below under "Hyperproliferative Disorders"), and disorders of	(e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular	dysfunction, atherosclerosis	and atherosclerotic vascular disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or	"Cardiovascular Disorders").	Highly preferred indications	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or
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preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications	include antiangiogenic activity to treat solid tumors,	sarcoma, and retinal disorders. Highly preferred indications	include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and	cavernous), glomus tumors,	angiomatosis,	hemangioendothelioma,	haemangiopericytoma,	lymphangioma,	preferred indications also	include cancers such as,	prostate, breast, lung, colon, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.
		-									*	-					
					-												

Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s phenomenom, ameurysms, restenosis, venous and lymphatic disorders such as thrombophlebitis, hymphatic disorders such as thrombophlebitis, hymphatic disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injury such as injury resulting from balloon angioplasty, and atteroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred	Highly preferred indications also include arterial disease, such as attenosolerosis, such as attenosolerosis, such as attenosolerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud's disease and Reynaud's disease and Reynaud's phenomenom, aneurysms, restenosis; venous and lymphanc disorders such as thrombophlebitis, lymphanci disorders such as thrombophlebitis, and lymphancialis, and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, searring, inschemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and ostepoporosis.																													
		Highly preferred indications also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred
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										** *******																		•••		

					as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
233	HHFEC49	1181	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, regulate	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include
				inflammatory activities, modulate TH2 helper cell	autoimmune disease (e.g., rheumatoid arthritis, systemic

	function, and/or mediate	lupus ervthematosis, multiple
	humoral or cell-mediated	sclerosis and/or as described
	immunity. Exemplary assays	below), immunodeficiency
	that test for	(e.g., as described below),
	immunomodulatory proteins	boosting a T cell-mediated
	evaluate the production of	immune response, and
	cytokines, such as Interferon	suppressing a T cell-mediated
	gamma (IFNg), and the	immune response. Additional
	activation of T cells. Such	highly preferred indications
	assays that may be used or	include inflammation and
	routinely modified to test	inflammatory disorders.
	immunomodulatory activity of	Additional preferred
	polypeptides of the invention	indications include idiopathic
	(including antibodies and	pulmonary fibrosis. Highly
	agonists or antagonists of the	preferred indications include
	invention) include the assays	neoplastic diseases (e.g.,
	disclosed in Miraglia et al., J	leukemia, lymphoma,
	Biomolecular Screening 4:193-	melanoma, and/or as described
-	204 (1999); Rowland et al.,	below under
	"Lymphocytes: a practical	"Hyperproliferative
	approach" Chapter 6:138-160	Disorders"). Highly preferred
	(2000); Gonzalez et al., J Clin	indications include neoplasms
	Lab Anal 8(5):225-233 (1995);	and cancers, such as, for
-	Billiau et al., Ann NY Acad	example, leukemia, lymphoma,
	Sci 856:22-32 (1998); Boehm	melanoma, and prostate,
	et al., Annu Rev Immunol	breast, lung, colon, pancreatic,
	15:749-795 (1997), and	esophageal, stomach, brain,
	Rheumatology (Oxford)	liver and urinary cancer. Other
	38(3):214-20 (1999), the	preferred indications include
	contents of each of which are	benign dysproliferative
	herein incorporated by	disorders and pre-neoplastic

				reference in its entirety. Human T cells that may be	conditions, such as, for example, hyperplasia,
				used according to these assays	metaplasia, and/or dysplasia.
				may be isolated using	Preferred indications include
				techniques disclosed herein or	anemia, pancytopenia,
				otherwise known in the art.	leukopenia, thrombocytopenia,
				Human T cells are primary	Hodgkin's disease, acute
				human lymphocytes that	lymphocytic anemia (ALL),
				mature in the thymus and	plasmacytomas, multiple
				express a T Cell receptor and	myeloma, Burkitt's lymphoma,
				CD3, CD4, or CD8. These	arthritis, AIDS, granulomatous
				cells mediate humoral or cell-	disease, inflammatory bowel
				mediated immunity and may	disease, sepsis, neutropenia,
				be preactivated to enhance	neutrophilia, psoriasis,
				responsiveness to	suppression of immune
				immunomodulatory factors.	reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HHFFJ48	1182	Activation of	Kinase assay. Kinase assays,	A highly preferred
234			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method

Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), neural disorders (e.g., as described below under ion "Neural Activity and Beart.	 retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g.,	due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,
fibroblast cells developed through clonal isolation and undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.		

nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional
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	complications associated with insulin resistance. Additional highly preferred
	insulin resistance. Additional highly preferre
	Additional highly preferre
	indications are disorders of the
	musculoskeletal systems
	including myopathies,
	muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include,
	hypertension, coronary artery
	disease, dyslipidemia,
	gallstones, osteoarthritis,
	degenerative arthritis, eating
	disorders, fibrosis, cachexia,
•	and kidney diseases or
	disorders. Highly preferred
	indications include neoplasms
	and cancer, such as, lipoma,
	liposarcoma, lymphoma,
	leukemia and breast, colon,
	and kidney cancer. Additional
•	highly preferred indications
	include melanoma, prostate,
	lung, pancreatic, esophageal,
	stomach, brain, liver, and
	urinary cancer. Other preferred
	indications include benign
	dysproliferative disorders and
	pre-neoplastic conditions, such

includes a method for stimulating (e.g., incre MCP-1 production. An alternative highly prefit embodiment of the invincludes a method for includes a method for inflammation (e.g., an infection (e.g., an infection (e.g., an infection inflammation and inflammation and inflammation and inflammatory disorder Preferred indications in blood disorders (e.g., a described below under "Immune Activity", "Immune Activity", "Immune Activity", "Immune Activity", "Highly preferred indications include autoinmanned and include and i	HHFGR93 HHFGR93	1183	SEAP in Alk Phos C2C12 Production of MCP-1	MCP-1 FMAT. Assays for immunomodulatory proteins	as, for example, hyperplasia, metaplasia, and/or dysplasia. A highly preferred embodiment of the invention
				that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce chemotaxis, and modulate immuno cell activation. Exemplary assays that test for immunomodulatory proteins evaluate the production of cell surface markers, such as monocyte chemoattractant protein (MCP), and the	includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-
		**		activation of monocytes and T cells. Such assays that may be used or routinely modified to test immunomodulatory and	Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases

tion systemic lupus erythematosis, multiple sclerosis and/or as f the described below) and	immunodeficiencies (e.g., as described below). Preferred 4:193- indications also include			nol arthritis, AIDS, granulomatous disease, inflammatory bowel					irt. meningitis (bacterial and viral), Lyme Disease, asthma,	n and allergy Preferred h, indications also include	n neoplastic diseases (e.g., and leukemia, lymphoma, and/or as		"Hyperproliferative	Disorders), riigniy prejerred indications include neoplasms
polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical annuach" Chanter 6:138-160	(2000); Satthaporn and Eremin, J R Coll Surg Ednb	Verhasselt et al., J Immunol 158.2919-2925 (1997) the	contents of each of which are herein incorporated by	reference in its entirety. Human dendritic cells that may	be used according to these	assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which,	when activated by antigen and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.	

and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Cancer, Wound Healing, and Inflamation. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach brain liver and
	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of epithhelial genes. Exemplary assays for transcription through the NFKB response element that may be used or routinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies
	Activation of transcription through NFKB response element in epithelial cells (such as HELA cells).
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	HHFGR93
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RANTES FMAT. Assays for immunomodulatory proteins	that induce chemotaxis of T	eosinophils are well known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	induce chemotaxis, and/or	mediate humoral or cell-	mediated immunity.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as RANTES,	and the induction of	chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-
Production of RANTES in	bronchial	epimenum cens								-																	-	
1183																												
HHFGR93						***						-			<u></u>												· <u>-</u>	
235																												

		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Infection, Inflammation, Atherosclerosis, Hypersensitivity, and Leukemias
204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407 (1995), the contents of each of which are herein incorporated by reference in its entirety. Epithelial cells were isolated from bronchia/trachea	humans who were free of known respiratory diseases. See Wu et al., Am Rev Respir Dis. 132(2):311-20 (1985), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. Cells normally have very low concentrations of cytosolic calcium compared to
		Calcium flux in immune cells (such as monocytes)
	 	1183
		HHFGR93
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minds higher extendellinger	calcium. Extracellular factors	can cause an influx of calcium,	leading to activation of	calcium responsive signaling	pathways and alterations in	cell functions. Exemplary	assays that may be used or	routinely modified to measure	calcium flux in immune cells	(such as monocytes) include	assays disclosed in: Chan, CC,	et al., J Pharmacol Exp Ther,	269(3):891-896 (1994);	Andersson, K, et al., Cytokine,	12(12):1784-1787 (2000);	Scully, SP, et al., J Clin Invest,	74(2) 589-599 (1984); and,	Sullivan, E, et al., Methods	Mol Biol, 114:125-133 (1999),	the contents of each of which	is herein incorporated by	reference in its entirety. Cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the THP-1 monocyte
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HHFHJ59 1184	Production of IL-10	cell line. Assays for production of IL-10	Highly preferred indications
	and activation of T-	and activation of T-cells are	include allergy and asthma.
93	cells.	well known in the art and may	Additional highly preferred indications include immine
		to assess the ability of	and hematopoietic disorders
		polypeptides of the invention	(e.g., as described below under
		(including antibodies and	"Immune Activity", and
		agonists or antagonists of the	"Blood-Related Disorders"),
		invention) to stimulate or	autoimmune diseases (e.g.,
		inhibit production of IL-10	rheumatoid arthritis, systemic
		and/or activation of T-cells.	lupus erythematosis, Crohn"s
		Exemplary assays that may be	disease, multiple sclerosis
		used or routinely modified to	and/or as described below),
		assess the ability of	immunodeficiencies (e.g., as
-		polypeptides and antibodies of	described below), boosting a T
		the invention (including	cell-mediated immune
		agonists or antagonists of the	response, and suppressing a T
		invention) to modulate IL-10	cell-mediated immune
		production and/or T-cell	response.
		proliferation include, for	
		example, assays such as	
		disclosed and/or cited in:	
		Robinson, DS, et al., "Th-2	
		cytokines in allergic disease"	
		Br Med Bull; 56 (4): 956-968	
		(2000), and Cohn, et al., "T-	
		helper type 2 cell-directed	
		therapy for asthma"	
		Pharmacology & Therapeutics;	
		88:187-196 (2000); the	

·	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A
contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral	blood lymphocytes isolated from cord blood. IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6
	Production of IL-6
	1185
	HHFHR32
	237

		h	has been linked to autoimmune	highly preferred indication is
		. j	disease, plasmacytomas,	the stimulation or enhancement
		ш	myelomas, and chronic	of mucosal immunity. Highly
			hyperproliferative diseases.	preferred indications include
•		Y	Assays for immunomodulatory	blood disorders (e.g., as
		<u>ਬ</u>	and differentiation factor	described below under
		[d]	proteins produced by a large	"Immune Activity", "Blood-
		i N	variety of cells where the	Related Disorders", and/or
		<u> </u>	expression level is strongly	"Cardiovascular Disorders"),
		7.	regulated by cytokines, growth	and infection (e.g., as
		at	factors, and hormones are well	described below under
		- - - - - - - - - - - - - - - - - -	known in the art and may be	"Infectious Disease"). Highly
		Ä	used or routinely modified to	preferred indications include
			assess the ability of	autoimmune diseases (e.g.,
		<u> </u>	polypeptides of the invention	rheumatoid arthritis, systemic
,	•	<u></u>	(including antibodies and	lupus erythematosis, multiple
		8	agonists or antagonists of the	sclerosis and/or as described
		<u> </u>	invention) to mediate	below) and
		. II	immunomodulation and	immunodeficiencies (e.g., as
		P	differentiation and modulate T	described below). Highly
		<u>.</u>	cell proliferation and function.	preferred indications also
		田	Exemplary assays that test for	include boosting a B cell-
		<u> </u>	immunomodulatory proteins	mediated immune response
		<u>မ</u>	evaluate the production of	and alternatively suppressing a
		<u> </u>	cytokines, such as IL-6, and	B cell-mediated immune
		<u> </u>	the stimulation and	response. Highly preferred
	 	<u>n</u>	upregulation of T cell	indications include
		<u>a</u>	proliferation and functional	inflammation and
		g	activities. Such assays that	inflammatory
		u	may be used or routinely	disorders. Additional highly
		ū	modified to test	preferred indications include

asthma and allergy. Highly preferred indications include neoplastic diseases (e.g., myeloma, plasmacytoma,	leukemia, lymphoma, melanoma, and/or as described below under "Hyperproliferative	Disorders"). Highly preferred indications include neoplasms and cancers, such as, myeloma, plasmacytoma, leukemia, lymphoma, melanoma, and	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred		anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease,
immunomodulatory and diffferentiation activity of polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-	204(1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Verhasselt et al., J Immunol 158:2919-2925	(1997), the contents of each of which are herein incorporated by reference in its entirety. Human dendritic cells that may	be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in	suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting natural killer cell proliferation. A highly preferred embodiment of the invention includes a method for stimulating natural killer cell differentiation. An alternative highly preferred embodiment of the invention includes a
		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation.
	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of Natural Killer Cell ERK Signaling Pathway.
	1186	,
	HHFOJ29	HHFOJ29
	238	238

includes a method inhibiting natural k differentiation. bodies described below un "Hyperproliferativo Disorders"), blood (e.g., as described and/or "Blood-Relb Disorders"), immu cog (e.g., as described Infections (e.g., as described infections (e.g., as described infections (e.g., as below under "Infections (e.g., as below under "Infections include disorders (e.g., as below under "Infections include disorders (e.g., as below under "Infections include disorders", and/or "Cardiovascular Disorders" as systemic lupus ery multiple sclerosis acells.	8	obe side to the bodies sits of the bodies sits of the ret of the side of the second se	oe of the bodies its of the ret 11101- of of of mal sed sed in its sed in its of sed in its of	ī	ler cell	Highly	include	s.g., as	er		isorders	low under		orders",	þ	disorders	low under	and	scribed	sno	red	lood	scribed	Je	elated		orders").	ications	diseases	hritis,	ematosis,	d/or as	7
inase activity that may be seed or routinely modified to est ERK kinase-induced activity of polypeptides of the nivention (including antibodies and agonists or antagonists of he invention) include the issays disclosed in Forrer et al., Biol Chem 379(8-9):1101-110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 1999); Chang and Karin, Vature 410(6824):37-40 2001); and Cobb MH, Prog Siophys Mol Biol 71(3-4):479-600 (1999); the contents of ach of which are herein ncorporated by reference in its mirety. Natural killer cells hat may be used according to hese assays are publicly vailable (e.g., through the ATCC). Exemplary natural ciller cells that may be used according to these assays nclude the human natural ciller cells that may be used according to these assays nclude the human natural ciller cell lines (for example, VK-YT cells which have sytolytic and cytotoxic activity) or primary NK cells.	kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have evtolytic and cytotoxic	kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998); Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have exposity or reimary NK cells	kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include the assays disclosed in Forrer et al., Biol Chem 379(8-9):1101-1110 (1998), Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by reference in its entirety. Natural killer cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary natural killer cells that may be used according to these assays include the human natural killer cell lines (for example, NK-YT cells which have cytolytic and cytotoxic	includes a method fo	inhibiting natural kill	differentiation. H	preferred indications	neoplastic diseases (described below und	"Hyperproliferative	Disorders"), blood di	(e.g., as described be	"Immune Activity",	"Cardiovascular Dise	and/or "Blood-Relate	Disorders"), immune	(e.g., as described be	"Immune Activity")	infections (e.g., as de	below under "Infecti	Disease"). Prefer	indications include b	disorders (e.g., as de	below under "Immu	Activity", "Blood-Re	Disorders", and/or	"Cardiovascular Disc	Highly preferred ind	include autoimmune	(e.g., rheumatoid artl	systemic lupus eryth	multiple sclerosis an	described below) and
S S S S S S S S S S S S S S S S S S S				kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Kyriakis JM,	Biochem Soc Symp 64:29-48	(1999); Chang and Karin,	Nature 410(6824):37-40	(2001); and Cobb MH, Prog	Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of	each of which are herein	incorporated by reference in its	entirety. Natural killer cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary natural	killer cells that may be used	according to these assays	include the human natural	killer cell lines (for example,	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.

described below). Additional highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications also include cancers such as, kidney, melanoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications	include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia (ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A highly preferred
		Kinase assay. Kinase assays,
		Activation of Ki
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		HHGB091

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embodiment of the invention includes a method for stimulating adipocyte	proliferation. An alternative highly preferred embodiment	of the invention includes a method for inhibiting	adipocyte proliferation. A	highly preferred embodiment	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").
for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell	proliferation or differentiation are well known in the art and	may be used or routinely modified to assess the ability	of polypeptides of the	invention (including antibodies	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and
Adipocyte ERK Signaling Pathway																									
239								7		156										i					

	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative			disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,		described below under	"Immune Activity",		and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), neural		below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as	described below under	"Infectious Disease").	A highly preferred indication	is diabetes mellitus. An	additional highly preferred	indication is a complication	associated with diabetes (e.g.,	dishetic retinonathy dishetic
Cobb MH, Prog Biophys Mol	Biol /1(3-4):4/9-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3	fibroblast cells developed	through clonal isolation and	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	conditions known in the art.									
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				-								-																		

nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired
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wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred
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indications include neoplasms and cancer, such as, lymphoma, leukemia and breast, colon, and kidney cancer. Additional preferred indications include melanoma, prostate, lung, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Highly preferred indications include lipomas and liposarcomas. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A 1: 11.	A nightly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),
		Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies.
	IL-10 in Human T-cell 293T	Stimulation of insulin secretion from pancreatic beta cells.
	1188	1188
	HHGCM76	HHGCM76
	240	240

			Insulin secretion from	diabetic neuropathy, nerve
		•	pancreatic beta cells is	disease and nerve damage
			upregulated by glucose and	(e.g., due to diabetic
			also by certain	neuropathy), blood vessel
			proteins/peptides, and	blockage, heart disease, stroke,
	112-20		disregulation is a key	impotence (e.g., due to diabetic
			component in diabetes.	neuropathy or blood vessel
			Exemplary assays that may be	blockage), seizures, mental
			used or routinely modified to	confusion, drowsiness,
			test for stimulation of insulin	nonketotic hyperglycemic-
			secretion (from pancreatic	hyperosmolar coma,
			cells) by polypeptides of the	cardiovascular disease (e.g.,
			invention (including antibodies	heart disease, atherosclerosis,
			and agonists or antagonists of	microvascular disease,
			the invention) include assays	hypertension, stroke, and other
			disclosed in: Ahren, B., et al.,	diseases and disorders as
			Am J Physiol, 277(4 Pt	described in the
			2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
			al., Endocrinology,	section below), dyslipidemia,
			138(9):3735-40 (1997); Kim,	endocrine disorders (as
			K.H., et al., FEBS Lett,	described in the "Endocrine
-			377(2):237-9 (1995); and,	Disorders" section below),
			Miraglia S et. al., Journal of	neuropathy, vision impairment
	, <u>.</u>		Biomolecular Screening,	(e.g., diabetic retinopathy and
			4:193-204 (1999), the contents	blindness), ulcers and impaired
			of each of which is herein	wound healing, and infection
			incorporated by reference in its	(e.g., infectious diseases and
			entirety. Pancreatic cells that	disorders as described in the
			may be used according to these	"Infectious Diseases" section
2-94-0-1			assays are publicly available	below, especially of the
			(e.g., through the ATCC)	urinary tract and skin), carpal

tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of Inflammation, Vascular Disease, Athereosclerosis, s Restenosis, and Stroke
and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays include rat INS-1 cells. INS-1 cells are a semi-adherent cell line established from cells isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for measuring expression of ICAM-1 are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate ICAM-1 expression. Exemplary assays that may be used or routinely modified to measure ICAM-1 expression include assays disclosed in: Takacs P, et al, FASEB J, 15(2):279-281
	Production of ICAM-1
	1188
	HHGCM76
	240

	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte
(2001); and, Miyamoto K, et al., Am J Pathol, 156(5):1733-1739 (2000), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to
	Activation of Adipocyte ERK Signaling Pathway
	1189
	HHGCQ54
	241

differentiation. A highly preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	"Hyperproliferative	Disorders"). Preferred	indications include blood	disorders (e.g., hypertension,	congestive heart failure, blood	vessel blockage, heart disease,	stroke, impotence and/or as	described below under	"Immune Activity",	/ "Cardiovascular Disorders",	and/or "Blood-Related
test ERK kinase-induced activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Mouse adipocyte cells that	may be used according to these	assays are publicly available	(e.g., through the ATCC).	Exemplary mouse adipocyte	cells that may be used	according to these assays	include 3T3-L1 cells. 3T3-L1	is an adherent mouse	preadipocyte cell line that is a	continuous substrain of 3T3
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	fibroblast cells developed	Disorders"), immune disorders
	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immune Activity"), neural
	adipose-like conversion under	disorders (e.g., as described
	appropriate differentiation	below under "Neural Activity
	conditions known in the art.	and Neurological Diseases"),
~		and infection (e.g., as
-3		described below under
		"Infectious Disease").
. —		A highly preferred indication
-		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
-		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
	-	neuropathy or blood vessel
 		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-

hyperosmolar coma, cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease, hypertension, stroke, and other	diseases and disorders as	described in the "Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders' section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with

Additional highly preferred	indications are disorders of the	including myonathies.	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,	prostate, lung, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer.	Highly preferred indications	include lipomas and	liposarcomas. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such
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242		1190	Activation of	Assays for the activation of	A preferred embodiment of
!			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
			`	the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
_				antagonists of the invention) to	production. Preferred
		• •		regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
-				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
				Proc Natl Acad Sci USA	suppressing a T cell-mediated
				85:6342-6346 (1988); and	immune response. Additional
				Black et al., Virus Genes	highly preferred indications
				12(2):105-117 (1997), the	include inflammation and

inflammatory disorders, and treating joint damage in patients with rheumatoid arthritis. An additional highly	Highly preferred indications Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative	highly preferred indications include neoplasms and cancers, such as, for example,	melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic,	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodokin's disease, acute
content of each of which are herein incorporated by reference in its entirety. T cells that may be used	according to these assays are publicly available (e.g., through the ATCC). Exemplary mouse T cells that may be used according to these assays include the CTLL cell	dependent suspension culture of T cells with cytotoxic activity.			
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	tra	transcription through the AP1	"Infectious Disease"). Highly
	res	response element that may be	preferred indications include
	9SN	used or routinely modified to	autoimmune diseases (e.g.,
	tes	test AP1-response element	rheumatoid arthritis, systemic
	act	activity of polypeptides of the	lupus erythematosis, multiple
	ni	invention (including antibodies	sclerosis and/or as described
	and	and agonists or antagonists of	below) and
	the	the invention) include assays	immunodeficiencies (e.g., as
	dis	disclosed in Berger et al., Gene	described below). Additional
	99	66:1-10 (1988); Cullen and	highly preferred indications
	Ma	Malm, Methods in Enzymol	include inflammation and
	21	216:362-368 (1992); Henthorn	inflammatory disorders.
	et	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85	85:6342-6346 (1988);	also include neoplastic
	Re	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	7.27	272(49):30806-30811 (1997);	lymphoma, and/or as described
		Chang et al., Mol Cell Biol	below under
-	18	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fre	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29	29(3):838-844 (1999), the	indications include neoplasms
	[00]	contents of each of which are	and cancers, such as, leukemia,
	hei	herein incorporated by	lymphoma, prostate, breast,
	ref	reference in its entirety.	lung, colon, pancreatic,
	H	Human T cells that may be	esophageal, stomach, brain,
	Sn	used according to these assays	liver, and urinary cancer. Other
	are	are publicly available (e.g.,	preferred indications include
	thr	through the ATCC).	benign dysproliferative
	Ex	Exemplary human T cells that	disorders and pre-neoplastic
	em	may be used according to these	conditions, such as, for
	ass	assays include the SUPT cell	example, hyperplasia,
	lin	line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.

			responsive suspension-culture cell line.	Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.
HHGDW43	1191	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell functions. Exemplary assays for transcription through the AP1 response element that may be used or routinely modified to test AP1-response element	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection (e.g., an infectious disease as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic

multiple escribed (e.g., as	dditional cations n and ers.	ications tic mia, s described	preferred neoplasms lenkemia	breast, tic, tic, brain, brain, tic, treer. Other sinclude ive	for a, ysplasia. s include DS, icytopenia, ocytopenia,
lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as	described below). Additional highly preferred indications include inflammation and inflammatory disorders.	Highly preferred indications also include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described	"Hyperproliferative "Hyperproliferative Disorders"). Highly preferred indications include neoplasms	Ilymphoma, prostate, breast, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, leukopenia, thrombocytopenia,
activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	n ne		Chang et al., Mol Cell Biol 18(9):4986-4993 (1998); and Fraser et al., Eur J Immunol 29(3):838-844 (1999), the	t 8	6)
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Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis, meningitis, and Lyme Disease.	Highly preferred indications include allergy and asthma. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune
	Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to assess the ability of polypeptides and antibodies of the invention (including agonists or antagonists of the invention) to modulate IL-10 production and/or T-cell proliferation include, for
	Production of IL-10 and activation of T-cells.
	1191
	HHGDW43
	243

example, assays such as disclosed and/or cited in: Robinson, DS, et al., "Th-2 cytokines in allergic disease" Br Med Bull; 56 (4): 956-968 (2000), and Cohn, et al., "Theherapy for asthma" Pharmacology & Therapeutics; 88: 187-196 (2000); the contents of each of which are herein incorporated by reference in their entirety. Exemplary cells that may be used according to these assays include Th2 cells. IL10 secreted from Th2 cells may be measured as a marker of Th2 cell activation. Th2 cells are a class of T cells that secrete IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2																													
	cells are generated via in viuo culture under Th2 polarizing conditions using peripheral	cells are generated via in vitro	asthma. Primary T helper 2	pathogenesis of allergy and	in the initiation and	of Th2 cells play a major role	differentiation and activation	Factors that induce	IL4, IL10, IL13, IL5 and IL6.	a class of T cells that secrete	cell activation. Th2 cells are	measured as a marker of Th2	secreted from Th2 cells may be	include Th2 cells. IL10	used according to these assays	Exemplary cells that may be	reference in their entirety.	herein incorporated by	contents of each of which are	88: 187-196 (2000); the	Pharmacology & Therapeutics;	therapy for asthma"	helper type 2 cell-directed	(2000), and Cohn, et al., "T-	Br Med Bull; 56 (4): 956-968	cytokines in allergic disease"	Robinson, DS, et al., "Th-2	disclosed and/or cited in:	example, assays such as
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				from cord blood.	
	HHPDX20	1192	Activation of	Assays for the activation of	A highly preferred indication
244			transcription	transcription through the	is obesity and/or complications
			through cAMP	cAMP response element are	associated with obesity.
	-		response element	well-known in the art and may	Additional highly preferred
			(CRE) in pre-	be used or routinely modified	indications include weight loss
			adipocytes.	to assess the ability of	or alternatively, weight gain.
				polypeptides of the invention	An additional highly preferred
				(including antibodies and	indication is diabetes mellitus.
				agonists or antagonists of the	An additional highly preferred
				invention) to increase cAMP,	indication is a complication
				regulate CREB transcription	associated with diabetes (e.g.,
				factors, and modulate	diabetic retinopathy, diabetic
				expression of genes involved	nephropathy, kidney disease
				in a wide variety of cell	(e.g., renal failure,
	·-			functions. For example, a	nephropathy and/or other
				3T3-L1/CRE reporter assay	diseases and disorders as
			-	may be used to identify factors	described in the "Renal
				that activate the cAMP	Disorders" section below),
				signaling pathway. CREB	diabetic neuropathy, nerve
				plays a major role in	disease and nerve damage
				adipogenesis, and is involved	(e.g., due to diabetic
				in differentiation into	neuropathy), blood vessel
				adipocytes. CRE contains the	blockage, heart disease, stroke,
				binding sequence for the	impotence (e.g., due to diabetic
				transcription factor CREB	neuropathy or blood vessel
				(CRE binding protein).	blockage), seizures, mental
				Exemplary assays for	confusion, drowsiness,
				transcription through the	nonketotic hyperglycemic-
				cAMP response element that	hyperosmolar coma,
				may be used or routinely	cardiovascular disease (e.g.,

				modified to test cAMP-	heart disease, atherosclerosis,
				response element activity of	microvascular disease,
				polypeptides of the invention	hypertension, stroke, and other
				(including antibodies and	diseases and disorders as
				agonists or antagonists of the	described in the
		··		invention) include assays	"Cardiovascular Disorders"
		.+		disclosed in Berger et al., Gene	section below), dyslipidemia,
~				66:1-10 (1998); Cullen and	endocrine disorders (as
				Malm, Methods in Enzymol	described in the "Endocrine
				216:362-368 (1992); Henthorn	Disorders" section below),
		15		et al., Proc Natl Acad Sci USA	neuropathy, vision impairment
				85:6342-6346 (1988); Reusch	(e.g., diabetic retinopathy and
				et al., Mol Cell Biol	blindness), ulcers and impaired
				20(3):1008-1020 (2000); and	wound healing, and infection
	<u></u>			Klemm et al., J Biol Chem	(e.g., infectious diseases and
	·			273:917-923 (1998), the	disorders as described in the
				contents of each of which are	"Infectious Diseases" section
				herein incorporated by	below, especially of the
				reference in its entirety. Pre-	urinary tract and skin), carpal
				adipocytes that may be used	tunnel syndrome and
		**		according to these assays are	Dupuytren's contracture).
			•	publicly available (e.g.,	Additional highly preferred
				through the ATCC) and/or	indications are complications
				may be routinely generated.	associated with insulin
	<u> </u>	•		Exemplary mouse adipocyte	resistance.
				cells that may be used	
	-			according to these assays	
				include 3T3-L1 cells. 3T3-L1	
				is an adherent mouse	
				preadipocyte cell line that is a	
				continuous substrain of 3T3	

		Lett 485(2-3): 122-126 (2000);	inhibiting (e.g., decreasing)
		Nor et al., J Vasc Res 37(3):	apoptosis of endothelial cells.
		209-218 (2000); and Karsan	A highly preferred
		and Harlan, J Atheroscler	embodiment of the invention
		Thromb 3(2): 75-80 (1996);	includes a method for
		the contents of each of which	stimulating angiogenisis. An
		are herein incorporated by	alternative highly preferred
		reference in its entirety.	embodiment of the invention
		Endothelial cells that may be	includes a method for
		used according to these assays	inhibiting angiogenesis. A
		are publicly available (e.g.,	highly preferred embodiment
		through commercial sources).	of the invention includes a
		Exemplary endothelial cells	method for reducing cardiac
		that may be used according to	hypertrophy. An alternative
		these assays include bovine	highly preferred embodiment
		aortic endothelial cells	of the invention includes a
	•	(bAEC), which are an example	method for inducing cardiac
		of endothelial cells which line	hypertrophy. Highly
		blood vessels and are involved	preferred indications include
		in functions that include, but	neoplastic diseases (e.g., as
		are not limited to,	described below under
,		angiogenesis, vascular	"Hyperproliferative
		permeability, vascular tone,	Disorders"), and disorders of
		and immune cell extravasation.	the cardiovascular system
			(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,
			cardiomyopathy, valvular
			regurgitation, left ventricular
	•		dysfunction, atherosclerosis
			and atherosclerotic vascular

disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,
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hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary	angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal.	stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease.	vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis,
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Ivmnhanoitis and
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lymphedema; and other
vascular disorders such as
peripheral vascular disease,
and cancer. Highly
preferred indications also
include trauma such as
wounds, burns, and injured
tissue (e.g., vascular injury
such as, injury resulting from
balloon angioplasty, and
atheroschlerotic lesions),
implant fixation, scarring,
ischemia reperfusion injury,
rheumatoid arthritis,
cerebrovascular disease, renal
diseases such as acute renal
failure, and osteoporosis.
Additional highly preferred
indications include stroke,
graft rejection, diabetic or
other retinopathies, thrombotic
and coagulative disorders,
vascularitis, lymph
angiogenesis, sexual disorders,
age-related macular
degeneration, and treatment
/prevention of endometriosis
and related conditions.
 Additional highly preferred
indications include fibromas,

					heart disease, cardiac arrest, heart valve disease, and vascular disease.
					blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory disorders (e.g., inflammatory bowel disease and Crohn's disease), and pain management.
244	HHPDX20	1192	IL-10 in Human T-cell 293T		
245	HHPGO40	1193	Proliferation of immune cells (such as the HMC-1 human mast cell	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in	Highly preferred indications include asthma, allergy, mastocytosis (a rare, heterogeneous disorder

characterized by excessive accumulation of mast cells, and their proliferation and action in the skin, central nervous system, and other organs). Preferred indications also include hematopoietic and immunological disorders (e.g., as described below under "Ilmnune Activity", and "Blood-Related Disorders"), infection (e.g., as described below under "Infectious Disease"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below), and			
the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of eosinophil cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. Mast cells are found in connective and mucosal tissues throughout the body. Mast cell activation (via immunoglobulin E-antigen, promoted by T helper cell type 2 cytokines) is an important component of allergic disease. Dysregulation of mast cell	apoptosis may play a role in allergic disease and mast cell tumor survival. Mast cell lines	tumor survival. Mast cell lines	
line)			

these assays are publicly available and/or may be routinely generated. Exemplary mast cells that may be used according to these assays include HMC-1, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be
	Glucose Production in H4IIE	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1193	1193
	HHPGO40	HHPGO40
	245	245

		Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.
used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.		Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for
	Caspase (+paclitaxel) in SW480	Regulation of apoptosis of immune cells (such as mast cells).
	1193	1194
,	HHPGO40	HHPTJ65
	245	246

example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation	via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an important component of allergic disease. Dysregulation of mast cell apoptosis may	play a role in allergic disease and mast cell tumor survival. Exemplary assays for caspase apoptosis that may be used or routinely modified to test capase apoptosis activity induced by polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the assays disclosed in: Masuda A, et al., J Biol Chem, 276(28):26107-26113 (2001); Yeatman CF 2nd, et al., J Exp Med, 192(8):1093-1103 (2000);Lee et al., FEBS Lett 485(2-3): 122-126 (2000): Nor	et al., J Vasc Res 37(3): 209- 218 (2000); and Karsan and Harlan, J Atheroscler Thromb 3(2): 75-80 (1996); the

ch are be used ys are urces). Is that to these Is such st cell							ssess preferred embodiment of the	des of invention includes a method			n) to		le disorders (e.g., as described		assays Activity", "Blood-Related	the Disorders", and/or		est SRE Highly preferred indications
contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through commercial sources). Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.		Assays for the activation of	transcription through the		n (SRE) are well-known in the		routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	regulate the serum response	factors and modulate the	expression of genes involved	in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE
	IL-2 in Human T-cell 2B9	Activation of	transcription	through serum	response element in	immune cells (such	as T-cells).											
	1194	1195										- 191		_				
	HHPT165	HHSDX28		-														
·	246	i c	247															

-	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),			suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications		(e.g., leukemia, lymphoma,		under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	filmors and prostate, breast
activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.				
																								_						
		,					_																							

					under "Infectious Disease").
	HHSDX28	1195	Production of TNF	TNFa FMAT. Assays for	A highly preferred
247			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
		,		and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
			×	immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
	·			and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications
				polypeptides of the invention	include inflammation and

Ginclinding antibodies and inflammatory disorders, and	the	 disclosed in Miraglia et al., J arthritis. An additional highly	Biomolecular Screening 4:193- preferred indication is sepsis.	 "Lymphocytes: a practical include neoplastic diseases	091	_	Immunol 28(11):3886-3890 under "Hyperproliferative	 Immunol 160(7):3585-3593 highly preferred indications	ſ	Immunol 158:2919-2925 cancers, such as, leukemia,	(1997); and Nardelli et al., J lymphoma, melanoma, glioma	Leukoc Biol 65:822-828 (e.g., malignant glioma), solid	(1999), the contents of each of tumors, and prostate, breast,	which are herein incorporated lung, colon, pancreatic,	by reference in its entirety. esophageal, stomach, brain,	Human dendritic cells that may liver and urinary cancer. Other	be used according to these preferred indications include	assays may be isolated using benign dysproliferative	techniques disclosed herein or disorders and pre-neoplastic	otherwise known in the art. conditions, such as, for	Human dendritic cells are example, hyperplasia,	antigen presenting cells in metaplasia, and/or dysplasia.	suspension culture, which, Preferred indications include	when activated by antigen anemia, pancytopenia,	and/or cytokines, initiate and leukopenia, thrombocytopenia,	upregulate T cell proliferation Hodgkin's disease, acute

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	This reporter assay measures activation of the GATA-3 include allergy, asthma, and signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the include blood disorders (e.g., activations also include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are well-known in the include blood disorders (e.g., activations are activations are activations of transcriptions are activations are activations are activations are activations are activations are activations are activations.
	Activation of This reporter assay med activation of the GATA through GATA-3 signaling pathway in H response element in immune cells (such immune cells (such as mast cells). Solution of GATA-3 cells has been linked to cytokine and chemokin production. Assays for activation of transcription of t
	trans trans throurespy imm as m
	HHSDX28
	247

the ability of polynentides of	Related Disorders", and/or
the invention (including	"Cardiovascular Disorders").
antibodies and agonists or	Preferred indications include
antagonists of the invention) to	autoimmune diseases (e.g.,
regulate GATA3 transcription	rheumatoid arthritis, systemic
factors and modulate	lupus erythematosis, multiple
expression of mast cell genes	sclerosis and/or as described
important for immune response	below) and
development. Exemplary	immunodeficiencies (e.g., as
assays for transcription	described below). Preferred
through the GATA3 response	indications include neoplastic
element that may be used or	diseases (e.g., leukemia,
routinely modified to test	lymphoma, melanoma,
GATA3-response element	prostate, breast, lung, colon,
activity of polypeptides of the	pancreatic, esophageal,
invention (including antibodies	stomach, brain, liver, and
and agonists or antagonists of	urinary tract cancers and/or as
the invention) include assays	described below under
disclosed in Berger et al., Gene	"Hyperproliferative
66:1-10 (1998); Cullen and	Disorders"). Other preferred
 Malm, Methods in Enzymol	indications include benign
216:362-368 (1992); Henthorn	dysproliferative disorders and
et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
Quant Biol 64:563-571 (1999);	Preferred indications include
Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,

multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, to hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. ine				=	stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method
14(6):4286-4294 (1994), the contents of each of which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.				Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell	proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess
	IgG in Human B cells	MCP-1 in HUVEC	TNFa in Human T-cell 293T	Activation of Endothelial Cell p38 or JNK	Signaling Pathway.
	1195	1195	1196	1196	
	HHSDX28	HHSDX28	HILCF66	HILCF66	
	247	247	248	248	

for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for	stimulating endothelial cell proliferation. An alternative	highly preferred embodiment of the invention includes a	endothelial cell proliferation. A highly preferred	embodiment of the invention includes a method for	stimulating apoptosis of endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	stimulating (e.g., increasing)	endothelial cell activation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing) the	activation of and/or	inactivating endothelial cells.
the ability of polypeptides of the invention (including antibodies and agonists or	antagonists of the invention) to promote or inhibit cell proliferation, activation, and	apoptosis. Exemplary assays for JNK and p38 kinase	routinely man may be used or routinely modified to test JNK and p38 kinase-induced	activity of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are nublicly available (e.g.
								_											

A highly preferred embodiment of the invention	includes a method for stimulating angiogenisis. An		embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac
through the ATCC). Exemplary endothelial cells	that may be used according to these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.								-										
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hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,
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telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other
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peripheral vascular disease, and cancer. Highly preferred indications also include trannan such as wounds, burns, and injured tissue (e.g., vascular nijured tissue (e.g., vascular nijury such as, injury resulting from balloon angioplasty, and atherosoherotic lesions), implant fixation, scarring, ischemia repeterfision injury, theumatoid arthritis, cerebrovascular disease, tenal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft respection, diabetic or other retiropathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related mecular degeneration, and treatment (prevention of endometriosis and related conditions. Additional highly preferred indications include fibromas, heart disease, cardia artest, heart disease, cardia artest, heart and desastic cardia artest, heart and desastic cardia artest, heart disease, and heart disease, and							_																				_				
	vascular disorders such as	ripheral vascular disease,		eferred indications also	clude trauma such as	ounds, burns, and injured	ssue (e.g., vascular injury	ch as, injury resulting from	ulloon angioplasty, and	heroschlerotic lesions),	uplant fixation, scarring,	chemia reperfusion injury,	eumatoid arthritis,	rebrovascular disease, renal	seases such as acute renal	ilure, and osteoporosis.	dditional highly preferred	dications include stroke,	aft rejection, diabetic or	her retinopathies, thrombotic	nd coagulative disorders,	scularitis, lymph	igiogenesis, sexual disorders,	ye-related macular	generation, and treatment	revention of endometriosis	nd related conditions.	dditional highly preferred	dications include fibromas,	eart disease, cardiac arrest,	heart valve disease, and
	va	<u>pe</u>	au	pre	inc	N N	tis	ms	ba	ath	ij.	isc	-rpe		dis	fai	Ad	ij.	gr	oth	an	va	an	ag	de	Id/	an	A	<u>ij</u>	he	he
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					Vasculal discuss.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
249	HJACG02	1197	MIP-1a in HMC		
	HJACG02	1197	Proliferation of pre-	Assays for the regulation (i.e.	
249			adipose cells (such	increases or decreases) of viability and proliferation of	
				cells in vitro are well-known in	
			-	the art and may be used or	
				routinely modified to assess	

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the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein	incorporated by reference in its entirety.		This reporter assay measures
		MCP-1 in HUVEC	Activation or
		1197	1197
		HJACG02	HJACG02
		249	

activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription	through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of	immunomodulatory genes. NFkB is important in the pathogenesis of asthma. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66-1-10 (1998). Cullen and
inhibition of transcription through NFKB response element in immune cells (such	as basophils).	
249		

Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85.6342 6346 (1988). March	et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of which are herein incorporated	by reference in its entirety. Cells were pretreated with SID supernatants or controls for 15-18 hours, and then 10 ng/mL	of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48 hours. Basophils that may be used according to these assays	are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally	established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res, 9:381-390	(1985); Blom et al., Eur J

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated suppressing a T cell-mediated
Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE activity of the polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1198
	HJACG30
	250

•		enes highly preferred indications	0	nich are inflammatory disorders, and	y treating joint damage in			says are preferred indication is sepsis.	g., Highly preferred indications	include neoplastic diseases	cells that (e.g., leukemia, lymphoma,		TLL cell under "Hyperproliferative	Disorders"). Additionally,	n culture highly preferred indications	oxic include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.
	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.													
					1																									

HJACG30 1198

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve diabetic neuropathy, blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain proteins/peptides, and disregulation is a key component in diabetes.
	Stimulation of insulin secretion from pancreatic beta cells.
	HJACG30
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blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemichyperosmolar coma, cardiovascular disease (e.g.	heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as described in the "Endocrine	Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection	(e.g., infectious diseases and disorders as described in the	"Infectious Diseases" section below, especially of the	tunnel syndrome and Dimiviten's contracture)	An additional highly preferred indication is obesity and/or	complications associated with	obesity. Additional highly nreferred indications include
Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic cells) by polypeptides of the	invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et	al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett,	377(2):237-9 (1995); and, Miraglia S et. al., Journal of	Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein	incorporated by reference in its entirety. Pancreatic cells that	may be used according to these assays are publicly available	(c.g., unough me ATCC) and/or may be routinely oenerated Exemplary	pancreatic cells that may be used according to these assays	include rat INS-1 cells. INS-1	cells are a semi-adherent cell

weight loss or alternatively, weight gain. Aditional highly preferred indications are complications associated with insulin resistance.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkins lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative conditions, such as, for
isolated from an X-ray induced rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin secretion. References: Asfari et al. Endocrinology 1992 130:167.	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test GAS-response element activity of polypeptides of the
	Activation of transcription through GAS response element in immune cells (such as T-cells).
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	HJBCU04
	251

	and aconiete or antaconiete of	moton locio and low derra locio
	and agomets of antagomets of	inclapiasia, aliu/oi uyspiasia.
	the invention) include assays	Preferred indications include
	disclosed in Berger et al., Gene	autoimmune diseases (e.g.,
	66:1-10 (1998); Cullen and	rheumatoid arthritis, systemic
 48-44	Malm, Methods in Enzymol	lupus erythematosis, multiple
	216:362-368 (1992); Henthorn	sclerosis and/or as described
	et al., Proc Natl Acad Sci USA	below), immunodeficiencies
	85:6342-6346 (1988);	(e.g., as described below),
	Matikainen et al., Blood	boosting a T cell-mediated
	93(6):1980-1991 (1999); and	immune response, and
	Henttinen et al., J Immunol	suppressing a T cell-mediated
	155(10):4582-4587 (1995), the	immune response. Additional
	contents of each of which are	preferred indications include
	herein incorporated by	inflammation and
	reference in its entirety.	inflammatory disorders.
	Exemplary mouse T cells that	Highly preferred indications
	may be used according to these	include blood disorders (e.g.,
	assays are publicly available	as described below under
	(e.g., through the ATCC).	"Immune Activity", "Blood-
	Exemplary T cells that may be	Related Disorders", and/or
	used according to these assays	"Cardiovascular Disorders"),
	include the CTLL cell line,	and infection (e.g., viral
 	which is a suspension culture	infections, tuberculosis,
	of IL-2 dependent cytotoxic T	infections associated with
	cells.	chronic granulomatosus
		disease and malignant
		osteoporosis, and/or an
 		infectious disease as described
		below under "Infectious
		Disease"). An additional
		preferred indication is

idiopathic pulmonary fibrosis. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and	HJBCU04 II.99 Production of IL.4 FMAT. Assays for A highly preferred immunomodulatory proteins secreted by TH2 cells that stimulate B cells, T cells, macrophages and mast cells macrophages and mast cells and promote polarization of CD4+ cells into TH2 cells are well known in the art and may be used or routinely modified reducing) IL.4 production. An alternative be used or routinely modified reducing) IL.4 production. An alternative method for inhibiting (e.g., increasing) includes a method for inhibiting (e.g., increasing) are to a seess the ability of this highly preferred indication includes asthma. A highly fincluding antihodies and includes asthma. A highly fincluding antihodies and includes asthma.
	HJBC 251

indication includes rhinitis. Additional highly preferred indications include inflammation and inflammatory disorders.	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, melanoma, and/or as described below under	"Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as for	example, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon, pancreatic,	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Preferred indications include blood disorders (e.g., as described below under	Related Disorders", and/or "Cardiovascular Disorders")
invention) to mediate immunomodulation, stimulate immune cells, modulate immune cell polarization, and/or mediate humoral or	cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-4, and	the stimulation of immune cells, such as B cells, T cells, macrophages and mast cells. Such assays that may be used	or routinely modified to test immunomodulatory activity of polypeptides of the invention	agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J. Biomolecular Screening 4.102	204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160	(2000); Gonzalez et al., J Clin Lab Anal 8(5):277-283 (1194); Yssel et al., Res Immunol	et al., Nat Immunol 1(3):257- 261 (2000): and van der Graaff
				<u> </u>			

251					
252	HJBCY35	1200	SEAP in 3T3L1		
757	HJBCY35	1200	Regulation of	Assays for the regulation of	A highly preferred indication
757			viability and	Viability and proliteration of	is diabetes mellitus. An
			proliteration of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
	, .			cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
		····		of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
				cells by polypeptides of the	cardiovascular disease (e.g.,
				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Friedrichsen BN,	diseases and disorders as

				et al Mol Endocrinol	described in the
				15(1)·136-48 (2001)· Huotari	"Cardiovascular Disorders"
				MA, et al., Endocrinology,	section below), dyslipidemia,
				139(4):1494-9 (1998); Hugl	endocrine disorders (as
				SR, et al., J Biol Chem 1998	described in the "Endocrine
				Jul 10;273(28):17771-9	Disorders" section below),
				(1998), the contents of each of	neuropathy, vision impairment
				which is herein incorporated	(e.g., diabetic retinopathy and
				by reference in its entirety.	blindness), ulcers and impaired
				Pancreatic cells that may be	wound healing, and infection
				used according to these assays	(e.g., infectious diseases and
				are publicly available (e.g.,	disorders as described in the
				through the ATCC) and/or	"Infectious Diseases" section
				may be routinely generated.	below, especially of the
				Exemplary pancreatic cells that	urinary tract and skin), carpal
				may be used according to these	tunnel syndrome and
				assays include rat INS-1 cells.	Dupuytren's contracture). An
				INS-1 cells are a semi-	additional highly preferred
				adherent cell line established	indication is obesity and/or
				from cells isolated from an X-	complications associated with
				ray induced rat transplantable	obesity. Additional highly
				insulinoma. These cells retain	preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
				130:167.	
	HJBCY35	1200	Activation of	Kinase assay. Kinase assays,	A highly preferred
252			Skeletal Mucle Cell	for example an GSK-3 kinase	embodiment of the invention
			PI3 Kinase	assay, for PI3 kinase signal	includes a method for

Signalling Pathway transduction that regulate increasing muscle cell survival	glucose metabolism and cell An alternative highly preferred	survivial are well-known in the embodiment of the invention	art and may be used or includes a method for	routinely modified to assess decreasing muscle cell	the ability of polypeptides of survival. A preferred	the invention (including embodiment of the invention	antibodies and agonists or includes a method for	antagonists of the invention) to stimulating muscle cell	promote or inhibit glucose proliferation. In a specific	metabolism and cell survival. embodiment, skeletal muscle	Exemplary assays for PI3 cell proliferation is stimulated.	kinase activity that may be An alternative highly preferred	used or routinely modified to embodiment of the invention	test PI3 kinase-induced activity includes a method for	of polypeptides of the inhibiting muscle cell	ntibodies	and agonists or antagonists of embodiment, skeletal muscle	the invention) include assays cell proliferation is inhibited.	disclosed in Forrer et al., Biol A preferred embodiment of	Chem 379(8-9):1101-1110 the invention includes a	 Diabetes 49(2):263-271 cell differentiation. In a	(2000); and Schreyer et al., specific embodiment, skeletal	Diabetes 48(8):1662-1666 muscle cell differentiation is	(1999), the contents of each of stimulated. An alternative	which are herein incorporated highly preferred embodiment	by reference in its entirety. of the invention includes a	Rat myoblast cells that may be method for inhibiting muscle	used according to these assays cell differentiation. In a	_
								A -						-															_

	·	through the ATCC). Exemplary rat myoblast cells that may be used according to these assays include L6 cells. L6 is an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuses to form multinucleated myotubes and striated fibers after culture in differentiation media.	muscle cell differentiation is inhibited. Highly preferred indications include disorders of the musculoskeletal system. Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), endocrine disorders (e.g., as described below under "Endocrine Disorders"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as described below under "Immune disorders (e.g., as described below under "Immune Activity"), and infection (e.g., as described below under "Infectious Disease"). An highly preferred indication is diabetes mellitus.	
			additional highly preferred	
			associated with diabetes (e.g.,	

nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g,	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired
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	wound healing, infections
	(e.g., infectious diseases and
	disorders as described in the
	"Infectious Diseases" section
	below, especially of the
	urinary tract and skin), carpal
	tunnel syndrome and
	Dupuytren's contracture).
	 An additional highly preferred
	indication is obesity and/or
 	complications associated with
	obesity. Additional highly
	preferred indications include
	weight loss or alternatively,
	weight gain. Additional
	highly preferred indications are
 	complications associated with
	insulin resistance.
	Additional highly preferred
	indications are disorders of the
	musculoskeletal system
 	including myopathies,
	 muscular dystrophy, and/or as
	described herein.
	Additional highly preferred
	indications include: myopathy,
	atrophy, congestive heart
	failure, cachexia, myxomas,
	fibromas, congenital
	cardiovascular abnormalities,
	heart disease, cardiac arrest,

heart valve disease, and vascular disease. Highly preferred indications include neoplasms and cancer, such as, rhabdomyoma, rhabdosarcoma, stomach, esophageal, prostate, and urinary cancer. Preferred indications also include breast, lung, colon, pancreatic, brain, and liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, hyperplasia, metaplasia, and/or dysplasia.		ation of A preferred embodiment of the invention includes a method for inhibiting (e.g., wn in the production. An alternative o assess highly preferred embodiment of the invention includes a method for stimulating (e.g., ists or increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described
		Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the
	IL-2 in Human T-cell 293T	Activation of transcription through serum response element in immune cells (such as natural killer cells).
	1201	1201
	HJMBI18	HJMBI18
	253	253

below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and
expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,
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	-									****													·							

cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues, hemophilia,	hypercoagulation, diabetes	mellitus, endocarditis,	meningitis, Lyme Disease,
which is a human natural killer cell line with cytolytic and extotoxic activity.																										
					-																		-			
								-		_		_														-

					cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious
					disease as described below under "Infectious Disease").
757	HJMBM38	1202	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
4C7		<u>-</u>	Apoptosis	caspase apoptosis are well known in the art and may be	embodiment of the invention includes a method for
				used or routinely modified to	stimulating endothelial cell
			_	assess the ability of	growth. An alternative highly
				polypeptides of the invention	preferred embodiment of the
				(including antibodies and	invention includes a method
		_		agonists or antagonists of the	for inhibiting endothelial cell
				invention) to promote caspase	growth. A highly preferred
				protease-mediated apoptosis.	embodiment of the invention
				Induction of apoptosis in	includes a method for
				endothelial cells supporting the	stimulating endothelial cell
				vasculature of tumors is	proliferation. An alternative
				associated with tumor	highly preferred embodiment
				regression due to loss of tumor	of the invention includes a
				blood supply. Exemplary	method for inhibiting
				assays for caspase apoptosis	endothelial cell proliferation.
				that may be used or routinely	A highly preferred
				modified to test capase	embodiment of the invention
				apoptosis activity of	includes a method for
				polypeptides of the invention	stimulating apoptosis of
				(including antibodies and	endothelial cells. An
				agonists or antagonists of the	alternative highly preferred
7				invention) include the assays	embodiment of the invention
				disclosed in Lee et al., FEBS	includes a method for

	6	inhibiting (e.g., decreasing)
	Nor et al., J Vasc Kes 37(3):	apoptosis of endothelial cells.
	209-218 (2000); and Karsan	A highly preferred
	 and Harlan, J Atheroscler	embodiment of the invention
	Thromb 3(2): 75-80 (1996);	includes a method for
	 the contents of each of which	stimulating angiogenisis. An
	are herein incorporated by	alternative highly preferred
	reference in its entirety.	embodiment of the invention
	Endothelial cells that may be	includes a method for
	used according to these assays	inhibiting angiogenesis. A
	are publicly available (e.g.,	highly preferred embodiment
-	through commercial sources).	of the invention includes a
•	 Exemplary endothelial cells	method for reducing cardiac
	that may be used according to	hypertrophy. An alternative
	these assays include bovine	highly preferred embodiment
	aortic endothelial cells	of the invention includes a
	(bAEC), which are an example	method for inducing cardiac
	of endothelial cells which line	hypertrophy. Highly
	blood vessels and are involved	preferred indications include
	in functions that include, but	neoplastic diseases (e.g., as
	are not limited to,	described below under
	angiogenesis, vascular	"Hyperproliferative
	permeability, vascular tone,	Disorders"), and disorders of
	and immune cell extravasation.	the cardiovascular system
-		(e.g., heart disease, congestive
-		heart failure, hypertension,
-		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
	!	and atherosclerotic vascular

			disease, diabetic nephropathy, intracardiac shunt, cardiac
			hypertrophy, myocardial
			infarction, chronic
			hemodynamic overload, and/or
			as described below under
			"Cardiovascular Disorders").
			Highly preferred indications
		_	include cardiovascular,
			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
			well as diseases of the vessels
			themselves, such as of the
			arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
		1	stimulate angiogenesis and/or
			cardiovascularization. Highly
-			preferred are indications that
			inhibit angiogenesis and/or
			cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
			to treat solid tumors,
•			leukemias, and Kaposi"s
	_		sarcoma, and retinal disorders.
			Highly preferred indications
			include neoplasms and cancer,
			anopasing Possesing

lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,
		-					-																							
													-																	

heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain	A highly preferred embodiment of the invention includes a method for stimulating MIP1a production. An alternative highly preferred embodiment of the invention
	MIP-1alpha FMAT. Assays for immunomodulatory proteins produced by activated dendritic cells that upregulate monocyte/macrophage and T cell chemotaxis are well
	Production of MIP1alpha
	1203
	HJMBT65
	255

	known in the art and may be	includes a method for
	used or routinely modified to	inhibiting (e.g., reducing)
	assess the ability of	MIP1a production. A highly
	polypeptides of the invention	preferred indication is
	(including antibodies and	infection (e.g., an infectious
	agonists or antagonists of the	disease as described below
	invention) to mediate	under "Infectious Disease").
 	immunomodulation, modulate	Preferred indications include
	chemotaxis, and modulate T	blood disorders (e.g., as
	cell differentiation. Exemplary	described below under
	assays that test for	"Immune Activity", "Blood-
	immunomodulatory proteins	Related Disorders", and/or
	evaluate the production of	"Cardiovascular Disorders").
	chemokines, such as	Highly preferred indications
	macrophage inflammatory	include autoimmune diseases
	protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
	the activation of	systemic lupus erythematosis,
10-2	monocytes/macrophages and T	multiple sclerosis and/or as
	cells. Such assays that may be	described below) and
	used or routinely modified to	immunodeficiencies (e.g., as
	test immunomodulatory and	described below). Additional
	chemotaxis activity of	highly preferred indications
	polypeptides of the invention	include inflammation and
	(including antibodies and	inflammatory disorders.
 -	agonists or antagonists of the	Preferred indications also
	invention) include assays	include anemia, pancytopenia,
	disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
	Biomolecular Screening 4:193-	Hodgkin's disease, acute
	204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	"Lymphocytes: a practical	plasmacytomas, multiple
	approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,

				(2000): Satthanorn and	arthritis. AIDS granulomatous
				Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
				45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
				al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,
				29 (2000); Verhasselt et al., J	suppression of immune
711				Immunol 158:2919-2925	reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
				upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
255	HJMBT65	1203	CD71 in Human T cells		
					and the state of t

HJMBW30 1204 Activation of transcription through NFKB transcription through NFKB response element in immune cells (such as T-cells). Assays for the transcription through NFKB response element in immune cells (such as seess the above polypeptides of (including anti agonists or art invention) to rate transcription for the modulate exprimentation of the modulate exprimentation of the polypeptides of (including anti agonists or anti invention) in transcription the modified to test response elemphage in the polypeptides of (including anti agonists or anti invention) including anti agonists or anti invention including anti agonists or anti invention including anti invention including et al., Proc Na et al., Proc Na et al., Proc Na	256	HJMBW30	1204	SEAP in ATP-3T3- L1		
transcription through NFKB response element in immune cells (such as T-cells).		HJMBW30	1204	Activation of	Assays for the activation of	Highly preferred indications
through NFKB response element in immune cells (such as T-cells).	256			transcription	transcription through the	include inflammation and
	<u>)</u>			through NFKB	NFKB response element are	inflammatory disorders.
				response element in	well-known in the art and may	Highly preferred indications
as T-cells).				immune cells (such	be used or routinely modified	include blood disorders (e.g.,
				as T-cells).	to assess the ability of	as described below under
					polypeptides of the invention	"Immune Activity", "Blood-
					(including antibodies and	Related Disorders", and/or
					agonists or antagonists of the	"Cardiovascular Disorders").
					invention) to regulate NFKB	Highly preferred indications
					transcription factors and	include autoimmune diseases
	-				modulate expression of	(e.g., rheumatoid arthritis,
Exemplary ass transcription the NFKB response may be used o modified to tear response elempholypeptides of (including antiagonists or antiany including antiagonists or antiany including					immunomodulatory genes.	systemic lupus erythematosis,
					Exemplary assays for	multiple sclerosis and/or as
					transcription through the	described below), and
may be used o modified to terresponse elem polypeptides o (including antiagonists or antinvention) including invention) including including including including including antiagonists or antinvention) including includ					NFKB response element that	immunodeficiencies (e.g., as
modified to tearesponse elempolypeptides o (including antiagonists or antinvention) including antianention) including antianention) including antianention) including antianention) including antianention) including antianention including antianential agonists or antianent					may be used or rountinely	described below). An
response elem polypeptides o (including anti agonists or ant invention) incl disclosed in B 66:1-10 (1998 Malm, Metho 216:362-368 (et al., Proc Na					modified to test NFKB-	additional highly preferred
polypeptides o (including anti agonists or anti invention) incl disclosed in B 66:1-10 (1998 Malm, Methor 216:362-368 (et al., Proc Na	-				response element activity of	indication is infection (e.g.,
(including antiagonists or antianonists or antianonists) invention) including antianonists or					polypeptides of the invention	AIDS, and/or an infectious
agonists or ant invention) incl disclosed in B 66:1-10 (1998 Malm, Methor 216:362-368 (et al., Proc Na					(including antibodies and	disease as described below
invention) incl disclosed in B 66:1-10 (1998 Malm, Methoc 216:362-368 (et al., Proc Na					agonists or antagonists of the	under "Infectious Disease").
disclosed in B 66:1-10 (1998 Malm, Methoo 216:362-368 (et al., Proc Na			4		invention) include assays	Highly preferred indications
66:1-10 (1998 Malm, Methoo 216:362-368 (et al., Proc Na					disclosed in Berger et al., Gene	include neoplastic diseases
Malm, Method 216:362-368 (et al., Proc Na					66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
216:362-368 (et al., Proc Na					Malm, Methods in Enzymol	lymphoma, and/or as described
et al., Proc Na					216:362-368 (1992); Henthorn	below under
					et al., Proc Natl Acad Sci USA	"Hyperproliferative
85:6342-6346					85:6342-6346 (1988); Black et	Disorders"). Highly preferred

indications include neoplasms	as, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS,	granulomatous disease,	inflammatory bowel disease,	sepsis, neutropenia,	neutrophilia, psoriasis,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	suppression of immune	reactions to transplanted
al., Virus Gnes 15(2):105-117 (1907): and Frascar et al	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.													47-		
				-										-															
	,																					-							

					organs, asthma and allergy.
256	HJMBW30	1204	SEAP in SW480		
757	HJPAD75	1205	Activation of T-	Kinase assay. JNK and p38 kinase assays for signal	Preferred indications include
/67	and the second		Signaling Pathway.	transduction that regulate cell	described below under
			,	proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
-				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
· <u>-</u>				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
				Chem 379(8-9):1101-1110	Highly preferred indications
				(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
				Kyriakis JM, Biochem Soc	lymphoma, and/or as described

To Manuelian of II -6				Cr. 64:30 40 (1000). Chang	holowy wodow
To Manuelian of II -6				3yiiip 04.23-40 (1333), Cilalig	Delow ulluci
To Manuelian of II -6				and Karin, Nature	"Hyperproliferative
				410(6824):37-40 (2001); and	Disorders"). Highly preferred
			_	Cobb MH, Prog Biophys Mol	indications include neoplasms
				Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
				the contents of each of which	lymphoma, prostate, breast,
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
				according to these assays are	preferred indications include
		31		publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
Production of II. 6				Exemplary mouse T cells that	conditions, such as, for
Production of II -6	•		•	may be used according to these	example, hyperplasia,
1205 Production of II_6				assays include the CTLL cell	metaplasia, and/or dysplasia.
1205 Production of II_6				line, which is an IL-2	Preferred indications include
1705 Production of II -6				dependent suspension-culture	arthritis, asthma, AIDS,
1205 Production of II -6				cell line with cytotoxic	allergy, anemia, pancytopenia,
1205 Production of II -6				activity.	leukopenia, thrombocytopenia,
1205 Production of II -6					Hodgkin"s disease, acute
1205 Production of II -6					lymphocytic anemia (ALL),
1205 Production of II -6					plasmacytomas, multiple
1705 Production of II -6					myeloma, Burkitt's lymphoma,
1205 Production of II -6					granulomatous disease,
1205 Production of II -6					inflammatory bowel disease,
1705 Production of II -6					sepsis, psoriasis, suppression
1205 Production of II -6					of immune reactions to
1705 Production of II -6					transplanted organs and
1205 Production of II -6					tissues, endocarditis,
1205 Production of II -6					meningitis, and Lyme Disease.
חבידו זה ווחוזיההההו לויבו	HJPAD75	1205	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred

257	by T cells and has strong	embodiment of the invention
	effects on B cells. IL-6	includes a method for
	participates in IL-4 induced	stimulating (e.g., increasing)
	IgE production and increases	IL-6 production. An alternative
	IgA production (IgA plays a	highly preferred embodiment
	role in mucosal immunity).	of the invention includes a
	IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	Deregulated expression of IL-6	reducing) IL-6 production. A
	has been linked to autoimmune	highly preferrred indication is
	disease, plasmacytomas,	the stimulation or enhancement
	myelomas, and chronic	of mucosal immunity. Highly
	hyperproliferative diseases.	preferred indications include
	Assays for immunomodulatory	blood disorders (e.g., as
	and differentiation factor	described below under
	proteins produced by a large	with "Immune Activity", "Blood-
	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
-	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response

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and alternatively suppressing a B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory	disorders.Additional highly	preferred indications include	asthma and allergy. Highly	preferred indications include	neoplastic diseases (e.g.,	myeloma, plasmacytoma,	leukemia, lymphoma,	melanoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, myeloma,	plasmacytoma, leukemia,	lymphoma, melanoma, and	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
evaluate the production of cytokines. such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that	may be used or routinely	modified to test	immunomodulatory and	diffferentiation activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000); and Verhasselt et al., J	Immunol 158:2919-2925	(1997), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in
																												-	
											****			-						-									

			`	suspension culture, which.	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia.
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
-					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
257	HJPAD75	1205	Glucose Production in H4IIE		
	HJPAD75	1205	Regulation of	Assays for the regulation of	A highly preferred
257			transcription	transcription through the FAS	indication is diabetes mellitus.
			through the FAS	promoter element are well-	An additional highly preferred
			promoter element	known in the art and may be	indication is a complication
	***		in hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
-				assess the ability of	diabetic retinopathy, diabetic
_				polypeptides of the invention	nephropathy, kidney disease
				(including antibodies and	(e.g., renal failure,
	The second secon				

		- 0				
nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below),	diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	confusion, drowsiness, nonketotic hyperglycemic- hyperosmolar coma,	cardiovascular disease (e.g., heart disease, atherosclerosis, microvascular disease, hypertension, stroke, and other	diseases and disorders as described in the "Cardiovascular Disorders" section below), dyslipidemia,	described in the "Endocrine Disorders" section below), neuropathy, vision impairment (e.g., diabetic retinopathy and blindness), ulcers and impaired wound healing, and infection
agonists or antagonists of the invention) to activate the FAS promoter element in a reporter construct and to regulate	transcription of FAS, a key enzyme for lipogenesis. FAS promoter is regulated by many transcription factors including	SREBP. Insulin increases FAS gene transcription in livers of diabetic mice. This stimulation of transcription is	also somewhat glucose dependent. Exemplary assays that may be used or routinely	modified to test for FAS promoter element activity (in hepatocytes) by polypeptides of the invention (including	antibodies and agonists or antagonists of the invention) include assays disclosed in Xiong, S., et al., Proc Natl	53 (2000); Roder, K., et al., Eur J Biochem, 260(3):743-51 (1999); Oskouian B, et al., Biochem J, 317 (Pt 1):257-65 (1996); Berger, et al., Gene 66:1-10 (1988); and. Cullen.

contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be used available (e.g., through the routinely generated. ATCC) and/or may be used according to these assays include rat liver may be used according to these weight loss or alternatively, assays include rat liver with glucocorticoids, insulin, or cAMP derivatives.		Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For
contents of each of which is herein incorporated by reference in its entirety. Hepatocytes that may be us according to these assays, s as H4IIE cells, are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary hepatocytes that may be used according to the assays include rat liver hepatoma cell line(s) inducing with glucocorticoids, insulii or cAMP derivatives.	[1]	1
	SEAP in HIB/CRE	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1205	1205
	HJPAD75	HJPAD75
	257	257

		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell
example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127- 133 (1974), which is herein incorporated by reference in its entirety.		Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess the ability of the polypeptides of the invention (including antibodies and agonists or
	IFNg in Human T- cell 2B9	Protection from Endothelial Cell Apoptosis.
	1205	1206
	HJPAD75	HJPCP42
	257	258

antagonists of the invention) to	growth. A highly preferred
inhibit caspase protease-	embodiment of the invention
mediated apoptosis.	includes a method for
Exemplary assays for caspase	stimulating endothelial cell
apoptosis that may be used or	proliferation. An alternative
routinely modified to test	highly preferred embodiment
caspase apoptosis rescue of	of the invention includes a
 polypeptides of the invention	method for inhibiting
(including antibodies and	endothelial cell proliferation.
agonists or antagonists of the	A highly preferred
invention) include the assays	embodiment of the invention
disclosed in Romeo et al.,	includes a method for
Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
(2000); Messmer et al., Br J	growth. An alternative highly
Pharmacol 127(7): 1633-1640	preferred embodiment of the
(1999); and J Atheroscler	invention includes a method
Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
the contents of each of which	growth. A highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
Endothelial cells that may be	stimulating apoptosis of
 used according to these assays	endothelial cells. An
are publicly available (e.g.,	alternative highly preferred
through commercial sources).	embodiment of the invention
Exemplary endothelial cells	includes a method for
that may be used according to	inhibiting (e.g., decreasing)
these assays include bovine	apoptosis of endothelial cells.
aortic endothelial cells	A highly preferred
(bAEC), which are an example	embodiment of the invention
of endothelial cells which line	includes a method for
blood vessels and are involved	stimulating angiogenisis. An

alternative highly preferred embodiment of the invention includes a method for includes a method for	highly preferred embodiment of the invention includes a method for reducing cardiac	hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac	preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension,	aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under
in functions that include, but are not limited to, angiogenesis, vascular	permeability, vascular tone, and immune cell extravasation.					
	·		-			

"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,
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																								474.4						

haemangiopericytoma, lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly	preferred indications also
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														16															

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				wounds, burns, and injured	—- р
				tissue (e.g., vascular injury	×
				such as, injury resulting from	mo.
			× 300 ×	balloon angioplasty, and	
	· •			atheroschlerotic lesions),	
				implant fixation, scarring,	
<u></u>				ischemia reperfusion injury,	.,
				rheumatoid arthritis,	
				cerebrovascular disease, renal	enal
	**-			diseases such as acute renal	al
				failure, and osteoporosis.	
				Additional highly preferred	 پر
				indications include stroke,	
				graft rejection, diabetic or	
				other retinopathies, thrombotic	botic
				and coagulative disorders,	
				vascularitis, lymph	
				angiogenesis, sexual disorders,	rders,
				age-related macular	
				degeneration, and treatment	ınt
				/prevention of endometriosis	sis
				and related conditions.	
				Additional highly preferred	þ
		• •••		indications include fibromas,	nas,
				heart disease, cardiac arrest,	st,
	_			heart valve disease, and	
				vascular disease. Preferred	rred
				indications include blood	
		·-		disorders (e.g., as described	eq
<u></u>				100	

Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	This reporter assay measures activation or inhibition of the NFkB signaling pathway in Ku812 human basophil cell line. Assays for the activation or inhibition of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including
	Activation or inhibition of transcription through NFKB response element in immune cells (such as basophils).
	1206
	HJPCP42
	258

antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate	expression of immunomodulatory genes. NFkB is important in the	Exemplary assays for transcription through the NFKB response element that	may be used or rountinely modified to test NFKB-response element activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and Malm, Methods in Enzymol	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Marone	et al, Int Arch Allergy Immunol 114(3):207-17 (1997), the contents of each of	which are herein incorporated by reference in its entirety.	Cells were pretreated with SID supernatants or controls for 15-
	.,									

	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a
18 hours, and then 10 ng/mL of TNF was added to stimulate the NFkB reporter. SEAP activity was measured after 48 hours. Basophils that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human basophil cell lines that may be used according to these assays include Ku812, originally established from a patient with chronic myelogenous leukemia. It is an immature prebasophilic cell line that can be induced to differentiate into mature basophils. See, Kishi et al., Leuk Res. 9:381-390 (1985); Blom et al., Eur J Immunol. 22:2025-32 (1992), where the contents of each are herein incorporated by reference in its entirety.	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity).
	Production of IL-6
	1208
	HKAAH36
	260

III6 induces cytotoxic T cells	method for inhibiting (e o
Deregulated expression of IL-6	reducing) IL-6 production. A
has been linked to autoimmune	highly preferrred indication is
disease, plasmacytomas,	the stimulation or enhancement
myelomas, and chronic	of mucosal immunity. Highly
hyperproliferative diseases.	preferred indications include
Assays for immunomodulatory	blood disorders (e.g., as
and differentiation factor	described below under
proteins produced by a large	"Immune Activity", "Blood-
variety of cells where the	Related Disorders", and/or
expression level is strongly	"Cardiovascular Disorders"),
regulated by cytokines, growth	and infection (e.g., as
factors, and hormones are well	described below under
 known in the art and may be	"Infectious Disease"). Highly
used or routinely modified to	preferred indications include
assess the ability of	autoimmune diseases (e.g.,
polypeptides of the invention	rheumatoid arthritis, systemic
(including antibodies and	lupus erythematosis, multiple
agonists or antagonists of the	sclerosis and/or as described
invention) to mediate	below) and
immunomodulation and	immunodeficiencies (e.g., as
differentiation and modulate T	described below). Highly
cell proliferation and function.	preferred indications also
Exemplary assays that test for	include boosting a B cell-
immunomodulatory proteins	mediated immune response
evaluate the production of	and alternatively suppressing a
cytokines, such as IL-6, and	B cell-mediated immune
the stimulation and	response. Highly preferred
upregulation of T cell	indications include
proliferation and functional	inflammation and
activities. Such assays that	inflammatory

sep infl infl infl infl infl infl infl infl	A highly preferred embodiment of the invention by a large includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for includes
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the immunomodulation, induce chemotaxis, and modulate immune cell activation
	Production of MCP-1
	1208
	НКААН36
	260

Exemplary assays that test for	inflammation and
 immunomodulatory proteins	inflammatory disorders.
evaluate the production of cell	Preferred indications include
 surface markers, such as	blood disorders (e.g., as
monocyte chemoattractant	described below under
protein (MCP), and the	"Immune Activity", "Blood-
activation of monocytes and T	Related Disorders", and/or
cells. Such assays that may be	"Cardiovascular Disorders").
used or routinely modified to	Highly preferred indications
test immunomodulatory and	include autoimmune diseases
diffferentiation activity of	(e.g., rheumatoid arthritis,
polypeptides of the invention	systemic lupus erythematosis,
(including antibodies and	multiple sclerosis and/or as
agonists or antagonists of the	described below) and
invention) include assays	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	described below). Preferred
Biomolecular Screening 4:193-	indications also include
204(1999); Rowland et al.,	anemia, pancytopenia,
"Lymphocytes: a practical	leukopenia, thrombocytopenia,
approach" Chapter 6:138-160	Hodgkin's disease, acute
(2000); Satthaporn and	lymphocytic anemia (ALL),
Eremin, J R Coll Surg Ednb	plasmacytomas, multiple
45(1):9-19 (2001); and	myeloma, Burkitt's lymphoma,
Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
158:2919-2925 (1997), the	disease, inflammatory bowel
contents of each of which are	disease, sepsis, neutropenia,
herein incorporated by	neutrophilia, psoriasis,
 reference in its entirety.	suppression of immune
Human dendritic cells that may	reactions to transplanted
be used according to these	organs and tissues,
assays may be isolated using	hemophilia, hypercoagulation,

				techniques disclosed herein or	diabetes mellitus, endocarditis,
				otherwise known in the art.	meningitis (bacterial and
				Human dendritic cells are	viral), Lyme Disease, asthma,
				antigen presenting cells in	and allergy Preferred
				suspension culture, which,	indications also include
				when activated by antigen	neoplastic diseases (e.g.,
				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
				upregulate T cell proliferation	described below under
			•	and functional activities.	"Hyperproliferative
		DECEMBER OF THE PROPERTY OF TH			Disorders"). Highly preferred
					indications include neoplasms
					and cancers, such as, leukemia,
					lymphoma, prostate, breast,
					lung, colon, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
			The state of the s	1000	metaplasia, and/or dysplasia.
260	HKAAH36	1208	IgG in Human B cells SAC		
	HKAAK02	1209	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
261				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
	-			IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a

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method for inhibiting (e.g., reducing) IL-6 production. A	highly preferred indication is the stimulation or enhancement	of mucosal immunity. Highly	preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	and infection (e.g., as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Highly	preferred indications also	include boosting a B cell-	mediated immune response	and alternatively suppressing a	B cell-mediated immune	response. Highly preferred	indications include	inflammation and	inflammatory
IL-6 induces cytotoxic T cells. Deregulated expression of IL-6	has been linked to autoimmune disease, plasmacytomas,	myelomas, and chronic	hyperproliferative diseases.	Assays for immunomodulatory	and differentiation factor	proteins produced by a large	variety of cells where the	expression level is strongly	regulated by cytokines, growth	factors, and hormones are well	known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to mediate	immunomodulation and	differentiation and modulate T	cell proliferation and function.	Exemplary assays that test for	immunomodulatory proteins	evaluate the production of	cytokines, such as IL-6, and	the stimulation and	upregulation of T cell	proliferation and functional	activities. Such assays that
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					• • •																							

		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
	-	including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign
		assays may be isolated using	dysproliferative disorders and
		techniques disclosed herein or	pre-neoplastic conditions, such
		otherwise known in the art.	as, for example, hyperplasia,
		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include
		suspension culture, which,	anemia, pancytopenia,
		when activated by antigen	leukopenia, thrombocytopenia,
		and/or cytokines, initiate and	Hodgkin's disease, acute
		upregulate T cell proliferation	lymphocytic anemia (ALL),
		and functional activities.	multiple myeloma, Burkitt's
			lymphoma, arthritis, AIDS,

granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease"). Additional highly preferred indications include
	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large variety of cells and act to induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and modulate immune cell activation.
	Production of MCP-1
	1209
	HKAAK02
	261

and trion sys for l to l				techniques disclosed herein or otherwise known in the art.	diabetes mellitus, endocarditis, meningitis (bacterial and
suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. In Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				Human dendritic cells are antigen presenting cells in	viral), Lyme Disease, asthma, and allergy Preferred
when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities. In Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				suspension culture, which,	indications also include
and/or cytokines, initiate and upregulate T cell proliferation and functional activities. In Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				when activated by antigen	neoplastic diseases (e.g.,
upregulate T cell proliferation and functional activities. 1210 Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				and/or cytokines, initiate and	leukemia, lymphoma, and/or as
and functional activities. Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				upregulate T cell proliferation	described below under
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase				and functional activities.	"Hyperproliferative
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					Disorders"). Highly preferred
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					indications include neoplasms
1210 Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					and cancers, such as, leukemia,
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					lymphoma, prostate, breast,
1210 Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					lung, colon, pancreatic,
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					esophageal, stomach, brain,
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					liver, and urinary cancer. Other
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					preferred indications include
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					benign dysproliferative
1210 Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					disorders and pre-neoplastic
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					conditions, such as, for
Endothelial Cell Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					example, hyperplasia,
Apoptosis Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase					metaplasia, and/or dysplasia.
caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote caspase	HKABI84	1210	Endothelial Cell	Caspase Apoptosis. Assays for	A highly preferred
be d to tion tion the pase			Apoptosis	caspase apoptosis are well	embodiment of the invention
d to tion tion the				known in the art and may be	includes a method for
tion the pase				used or routinely modified to	stimulating endothelial cell
tion tion the				assess the ability of	growth. An alternative highly
the				polypeptides of the invention	preferred embodiment of the
the				(including antibodies and	invention includes a method
			,	agonists or antagonists of the	for inhibiting endothelial cell
				invention) to promote caspase	growth. A highly preferred

ambodiment of the invention	includes a mathod for	includes a method for	stimulating endothelial cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting	endothelial cell proliferation.	A highly preferred	embodiment of the invention	includes a method for	stimulating apoptosis of	endothelial cells. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting (e.g., decreasing)	apoptosis of endothelial cells.	A highly preferred	embodiment of the invention	includes a method for	stimulating angiogenisis. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting angiogenesis. A	highly preferred embodiment	of the invention includes a	method for reducing cardiac	hypertrophy. An alternative	highly preferred embodiment
Cinctuctor to	protease-mediated apoptosis.	Induction of apoptosis in	endothelial cells supporting the	vasculature of tumors is	associated with tumor	regression due to loss of tumor	blood supply. Exemplary	assays for caspase apoptosis	that may be used or routinely	modified to test capase	apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Lee et al., FEBS	Lett 485(2-3): 122-126 (2000);	Nor et al., J Vasc Res 37(3):	209-218 (2000); and Karsan	and Harlan, J Atheroscler	Thromb 3(2): 75-80 (1996);	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through commercial sources).	Exemplary endothelial cells	that may be used according to	these assays include bovine
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of the invention includes a method for inducing cardiac hypertrophy. Highly	preferred indications include neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the
aortic endothelial cells (bAEC), which are an example of endothelial cells which line	blood vessels and are involved in functions that include, but	are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.																					
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	arteries canillaries veins
	atteries, capitatios, veins
	and/or lymphatics). Highly
	preferred are indications that
	stimulate angiogenesis and/or
_	cardiovascularization. Highly
	preferred are indications that
	inhibit angiogenesis and/or
	cardiovascularization.
	Highly preferred indications
	include antiangiogenic activity
	to treat solid tumors,
	leukemias, and Kaposi"s
	sarcoma, and retinal disorders.
	Highly preferred indications
	include neoplasms and cancer,
	such as, Kaposi"s sarcoma,
	hemangioma (capillary and
	cavernous), glomus tumors,
	telangiectasia, bacillary
	angiomatosis,
	hemangioendothelioma,
	angiosarcoma,
	haemangiopericytoma,
	lymphangioma,
	lymphangiosarcoma. Highly
	preferred indications also
	include cancers such as,
	prostate, breast, lung, colon,
	pancreatic, esophageal,
	stomach, brain, liver, and
,	urinary cancer. Preferred

indications include benign dysproliferative disorders and pre-neoplastic conditions, such	as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications	also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud''s	disease and Keynaud's phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombonhlebitis.	lymphangitis, and lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,

	cerebrovascular disease, renal
	diseases such as acute renal
	failure, and osteoporosis.
	Additional highly preferred
	indications include stroke,
 	graft rejection, diabetic or
	other retinopathies, thrombotic
	and coagulative disorders,
	vascularitis, lymph
,	angiogenesis, sexual disorders,
_	age-related macular
	degeneration, and treatment
	/prevention of endometriosis
	and related conditions.
	Additional highly preferred
	indications include fibromas,
	heart disease, cardiac arrest,
	heart valve disease, and
	vascular disease.
	Preferred indications include
•	blood disorders (e.g., as
	described below under
	"Immune Activity", "Blood-
	Related Disorders", and/or
	"Cardiovascular Disorders").
	Preferred indications include
	autoimmune diseases (e.g.,
	rheumatoid arthritis, systemic
 	lupus erythematosis, multiple
	sclerosis and/or as described
	helowy) and

immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders. An
	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions. Exemplary assays for transcription through the NFAT response element that may be used or routinely modified to test NFAT-response element activity of
	Activation of transcription through NFAT response in immune cells (such as T-cells).
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	HKABI84
	262

polypeptides of the invention additional highly preferred finelinding antibodies and indication is infection (e.g. an	the	invention) include assays below under "Infectious	disclosed in Berger et al., Gene Disease"). Preferred	66:1-10 (1998); Cullen and indications include neoplastic	Malm, Methods in Enzymol diseases (e.g., leukemia,	216:362-368 (1992); Henthorn lymphoma, and/or as described	 85:6342-6346 (1988); Serfling '"Hyperproliferative	 1498(1):1-18 (2000); De Boer indications include neoplasms	et al., Int J Biochem Cell Biol and cancers, such as, for	 Fraser et al., Eur J Immunol and prostate, breast, lung,	29(3):838-844 (1999); and colon, pancreatic, esophageal,	Yeseen et al., J Biol Chem stomach, brain, liver and	268(19):14285-14293 (1993), urinary cancer. Other preferred	the contents of each of which indications include benign	are herein incorporated by dysproliferative disorders and	reference in its entirety. T pre-neoplastic conditions, such	cells that may be used as, for example, hyperplasia,	according to these assays are metaplasia, and/or dysplasia.	publicly available (e.g., Preferred indications also	through the ATCC).	Exemplary human T cells that leukopenia, thrombocytopenia,	may be used according to these Hodgkin's disease, acute	assays include the JURKAT lymphocytic anemia (ALL),	cell line, which is a suspension plasmacytomas, multiple	culture of lenkemia cells that myeloma Burkitt's lymphoma	
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HKAB184 1210 Activation of transcription through the include inflammatory disperse including antibodies and ranscription through the immune cells (such be used or routinely modified as T-cells). HKAB184 1210 Activation of transcription through the transcription through the include inflammation and immune cells (such be used or routinely modified as T-cells). Assays for the activation of transcription through the include inflammation and immune cells (such be used or routinely modified as assess the ability of or assess the ability of include blood disorders (e.g. including antibodies and ranscription factors and modified to test NFKB immunonedulatory genes. Exemplary assays for modulatory genes. Exemplary assays for including antibodies and disciplinal include autoimmune discanding multiple sclerosis and or a described below). An modified to test NFKB-indiciplinal discanding antibodies and discanding antibodies and discanding antibodies and additional highly preferred indication include autoimmune discanding antibodies and antib						disease, inflammatory bowel
1210 Activation of transcription through the through NFKB response element in mell-known in the art and may immune cells (such as T-cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and						disease, sepsis, neutropenia, neutrophilia, psoriasis.
Activation of transcription through the through NFKB response element are response element in immune cells (such as T-cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and including antibodies and						suppression of immune
transcription through the transcription through NFKB response element in immune cells (such as T-cells). Polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and					-	reactions to transplanted
transcription through the transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and including antibodies and including antibodies and (including antibodies and (including antibodies and						organs and tissues,
transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB- response element activity of polypeptides of the invention (including antibodies and including antibodies and including antibodies and						hemophilia, hypercoagulation,
transcription through NFKB transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention of including antibodies and agonists or antagonists of the invention of including antibodies and agonists or antagonists of the invention of including actions and invention) to regulate NFKB transcription factors and inmunomodulatory genes. Exemplary assays for modulate expression of immunomodulatory genes. Exemplary assays for mytranscription through the down of the invention of including antibodies and in may be used or rountinely and modified to test NFKB-are response element that in may be used or rountinely and including antibodies and diffincluding antibodies and difficulting antibodies and diffincluding antibodies an						diabetes mellitus, endocarditis,
transcription through NFKB tresponse element in immune cells (such as T-cells). polypeptides of the invention of invention) to regulate NFKB transcription factors and may him only as agonists or antagonists of the invention invention of immunomodulatory genes. Exemplary assays for transcription through the modified to test NFKB-may be used or rountinely and modified to test NFK						meningitis, Lyme Disease,
transcription through NFKB response element in immune cells (such as T-cells). polypeptides of the invention of including antibodies and gonists or antagonists of the invention of immunomodulatory genes. Exemplary assays for transcription through the immunomodulatory genes. Exemplary assays for transcription through the immunomodulatory genes. Exemplary assays for transcription through the may be used or rountinely an modified to test NFKB-asponse element that in modified to test NFKB-asponse element activity of including antibodies and modified to test NFKB-asponse element activity of including antibodies and dincluding antibodies and dincluding antibodies and dincluding antibodies and difference in the polypeptides of the invention A dincluding antibodies and difference in the polypeptides and difference in the properties and dincluding antibodies and difference in the polypeptides and difference in the properties and difference in the properties and dincluding antibodies and difference in the properties and difference in the properti						asthma and allergy.
transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	_	HKABI84	1210	Activation of	Assays for the activation of	Highly preferred indications
NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				transcription	transcription through the	include inflammation and
well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				through NFKB	NFKB response element are	inflammatory disorders.
be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				response element in	well-known in the art and may	Highly preferred indications
to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and				immune cells (such	be used or routinely modified	include blood disorders (e.g.,
				as T-cells).	to assess the ability of	as described below under
			~		polypeptides of the invention	"Immune Activity", "Blood-
			-		(including antibodies and	Related Disorders", and/or
					agonists or antagonists of the	"Cardiovascular Disorders").
					invention) to regulate NFKB	Highly preferred indications
					transcription factors and	include autoimmune diseases
					modulate expression of	(e.g., rheumatoid arthritis,
					immunomodulatory genes.	systemic lupus erythematosis,
					Exemplary assays for	multiple sclerosis and/or as
					transcription through the	described below), and
					NFKB response element that	immunodeficiencies (e.g., as
					may be used or rountinely	described below). An
					modified to test NFKB-	additional highly preferred
					response element activity of	indication is infection (e.g.,
					polypeptides of the invention	AIDS, and/or an infectious
					(including antibodies and	disease as described below

agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117 (1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	under "Infectious Disease"). Highly preferred indications include neoplastic diseases (e.g., melanoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms	and cancers, such as, for example, melanoma, renal cell carcinoma, leukemia, lymphoma, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel
	agonists or antagonists of the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Black et al., Virus Gnes 15(2):105-117	(1997); and Fraser et al., 29(3):838-844 (1999), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	

					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
	27.7				suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HKABZ65	1211	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
263				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
	-			IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
	•			role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
-				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
-				regulated by cytokines, growth	and infection (e.g., as
		·		factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,

	polypeptides of the invention (including antibodies and	rheumatoid arthritis, systemic lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	cell proliferation and finction	described below). Highly preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
-	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	Iymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,

				which are herein incorporated	pancreatic, esophageal,
				by reference in its entirety.	stomach, brain, liver and
				Human dendritic cells that may	urinary cancer. Other preferred
				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		-	-		reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
				-	meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
HKAB	ABZ65	1211	Activation of	Kinase assay. JNK and p38	A highly preferred

kinase assays for signal embodiment of the invention	transduction that regulate cell includes a method for	proliferation, activation, or stimulating endothelial cell	apoptosis are well known in growth. An alternative highly	the art and may be used or preferred embodiment of the	routinely modified to assess invention includes a method	٠	the invention (including growth. A highly preferred	antibodies and agonists or embodiment of the invention	antagonists of the invention) to includes a method for	promote or inhibit cell stimulating endothelial cell	proliferation, activation, and proliferation. An alternative	apoptosis. Exemplary assays highly preferred embodiment	for JNK and p38 kinase of the invention includes a	activity that may be used or method for inhibiting	routinely modified to test JNK endothelial cell proliferation.	and p38 kinase-induced A highly preferred	activity of polypeptides of the embodiment of the invention	invention (including antibodies includes a method for	and agonists or antagonists of stimulating apoptosis of	the invention) include the endothelial cells. An	assays disclosed in Forrer et alternative highly preferred	al., Biol Chem 379(8-9):1101- embodiment of the invention	1110 (1998); Gupta et al., Exp includes a method for	Cell Res 247(2): 495-504 inhibiting (e.g., decreasing)	(1999); Kyriakis JM, Biochem apoptosis of endothelial cells.	Soc Symp 64:29-48 (1999); A highly preferred	Chang and Karin, Nature embodiment of the invention	410(6824):37-40 (2001); and includes a method for	Cobb MH, Prog Biophys Mol stimulating (e.g., increasing)
Endothelial Cell kin	p38 or JNK trar	Signaling Pathway. pro		the	ron	the	the	ant	ant	pro	pro	apo	for	acti	ron	and	acti	vni	and	the	ass	al.,	111	Cel	(19	Soc	Ch	410	Col
																			-										
263																													

the contents of each of which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells (HUVEC), which are endothelial cells (include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation and immune cell extravasation		by embodiment of the invention	includes a method for	y be inhibiting (e.g., decreasing) the	assays activation of and/or	g., inactivating endothelial cells.	A highly preferred	ells embodiment of the invention	ing to includes a method for			embodiment of the invention	ine includes a method for	d are inhibiting angiogenesis. A		ed to, of the invention includes a	method for reducing cardiac	me, hypertrophy. An alternative	sation. highly preferred embodiment	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,
	the contents of each of which	are herein incorporated by	reference in its entirety.	Endothelial cells that may be	used according to these	are publicly available (e.	through the ATCC).	Exemplary endothelial c	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.												
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			cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular
			disease, diabetic nephropathy,
		***	intracardiac shunt, cardiac
			hypertrophy, myocardial
			infarction, chronic
			hemodynamic overload, and/or
			as described below under
			"Cardiovascular Disorders").
			Highly preferred indications
			include cardiovascular,
***************************************			endothelial and/or angiogenic
			disorders (e.g., systemic
			disorders that affect vessels
			such as diabetes mellitus, as
		-	well as diseases of the vessels
		-	themselves, such as of the
			arteries, capillaries, veins
			and/or lymphatics). Highly
			preferred are indications that
		10-11-11	stimulate angiogenesis and/or
			cardiovascularization. Highly
			preferred are indications that
			inhibit angiogenesis and/or
			cardiovascularization.
			Highly preferred indications
			include antiangiogenic activity
	.,		to treat solid tumors,
			lenkemise and Kanoci"s

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sarcoma, and retinal disorders.	tions	include neoplasms and cancer,	ma,	and	nors,			•				lymphangiosarcoma. Highly	OS	•	olon,		pu	ğ	ign	dysproliferative disorders and	pre-neoplastic conditions, such	lasia,	lasia.	tions	ease,	•	hypertension, coronary artery			
nal dis	indica	s and	sarco	illary	us tun	cillary		lioma		toma,		ma. E	ons al	uch as	ung, c	ageal,	iver, a	eferre	le beni	isorde	ndition	yperp	r dysp	indica	ial dise	erosis	onary	tory	and"s	and"s
nd reti	erred	plasm	posi"s	ıa (cap	glom,	sia, ba	is,	ndothe	na,	pericy	ma,	sarco	dicati	cers sı	east, lı	esoph	rain, 1	cer. Pı	includ	ative d	tic co	nple, h	and/o	erred	arteri	eroscl	n, coi	lamme	, Reyr	Reyn
ma, aı	Highly preferred indications	de nec	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	hangic	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	olifera	eoplas	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	tensio	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s
sarco	High	inclu	snch	hema	caver	telang	angio	hema	angio	haem	lymp	lymp	prefe	inclu	prosta	pancr	stoms	urina	indica	dyspr	pre-n	as, fo	metal	Highl	also i	snch	hyper	disea	vascu	disea
				U-4.																										
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					/prevention of endometriosis
					and related conditions.
					Additional highly preferred
					indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease.
					Preferred indications include
					blood disorders (e.g., as
					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
	47-				preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
890	HKABZ65	1211	Regulation of	Caspase Apoptosis. Assays for caspase apontosis are well	A highly preferred indication is diabetes mellitus
201			apoptosis III	tot caspase apoptosis are well	וותוכמות וז מומסכוכי וווכוווומים:

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An additional highly preferred	indication is a complication	associated with diabetes (e.g.,	diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine
known in the art and may be	used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote caspase	protease-mediated apoptosis.	Apoptosis in pancreatic beta is	associated with induction and	progression of diabetes.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in: Loweth, AC, et	al., FEBS Lett, 400(3):285-8	(1997); Saini, KS, et al.,	Biochem Mol Biol Int,	39(6):1229-36 (1996);	Krautheim, A., et al., Br J	Pharmacol, 129(4):687-94	(2000); Chandra J, et al.,	Diabetes, 50 Suppl 1:S44-7	(2001); Suk K, et al., J	Immunol, 166(7):4481-9	(2001); Tejedo J, et al., FEBS
pancreatic beta	cells.			-													-												1-1-1-1	
			-											1	168					-									· <u>·</u>	

		Lett, 459(2):238-43 (1999);	Disorders" section below),
		Zhang, S., et al., FEBS Lett,	neuropathy, vision impairment
		455(3):315-20 (1999); Lee et	(e.g., diabetic retinopathy and
		al., FEBS Lett 485(2-3): 122-	blindness), ulcers and impaired
 		126 (2000); Nor et al., J Vasc	wound healing, and infection
		Res 37(3): 209-218 (2000);	(e.g., infectious diseases and
-		and Karsan and Harlan, J	disorders as described in the
**		Atheroscler Thromb 3(2): 75-	"Infectious Diseases" section
		80 (1996); the contents of each	below, especially of the
		of which are herein	urinary tract and skin), carpal
		incorporated by reference in its	tunnel syndrome and
		entirety. Pancreatic cells that	Dupuytren's contracture).
		may be used according to these	An additional highly preferred
	-	assays are publicly available	indication is obesity and/or
		(e.g., through the ATCC)	complications associated with
		and/or may be routinely	obesity. Additional highly
		generated. Exemplary	preferred indications include
	- 11	pancreatic cells that may be	weight loss or alternatively,
		used according to these assays	weight gain. Aditional
		include RIN-m. RIN-m is a	highly preferred indications are
		rat adherent pancreatic beta	complications associated with
		cell insulinoma cell line	insulin resistance.
 		derived from a radiation	
		induced transplantable rat islet	
		cell tumor. The cells produce	
		and secrete islet polypeptide	
 •		hormones, and produce insulin,	
		somatostatin, and possibly	
		glucagon. ATTC: #CRL-2057	
	-	Chick et al. Proc. Natl. Acad.	
		Sci. 1977 74:628; AF et al.	

				Proc. Natl. Acad. Sci. 1980	
				77:3519.	
	HKACB56	1212	Myoblast cell	Assays for muscle cell	Highly preferred indications
264			proliferation	proliferation are well known in	include diabetes, myopathy,
				the art and may be used or	muscle cell atrophy, cancers of
				routinely modified to assess	muscle (such as,
				the ability of polypeptides of	rhabdomyoma, and
				the invention (including	rhabdosarcoma),
				antibodies and agonists or	cardiovascular disorders (such
				antagonists of the invention) to	as congestive heart failure,
				stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
				cell proliferation. Exemplary	congenital cardiovascular
				assays for myoblast cell	abnormalities, heart disease,
				proliferation that may be used	cardiac arrest, heart valve
				or routinely modified to test	disease, vascular disease, and
				activity of polypeptides and	also as described below under
				antibodies of the invention	"Cardiovascular Disorders"),
				(including agonists or	stimulating myoblast
				antagonists of the invention)	proliferation, and inhibiting
				include, for example, assays	myoblast proliferation.
				disclosed in: Soeta, C., et al.	
				"Possible role for the c-ski	
				gene in the proliferation of	
				myogenic cells in regenerating	
				skeletal muscles of rats" Dev	
				Growth Differ Apr;43(2):155-	
			•	64 (2001); Ewton DZ, et al.,	
				"IGF binding proteins-4, -5	
				and -6 may play specialized	
				roles during L6 myoblast	
			The state of the s	proliferation and	

			differentiation" J Endocrinol Mar;144(3):539-53 (1995); and, Pampusch MS, et al., "Effect of transforming growth factor beta on proliferation of L6 and embryonic porcine myogenic cells" J Cell Physiol Jun;143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety.	
			may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	
HKACB56	1212	SEAP in HIB/CRE		
HKACB56	1212	CD152 in Human T cells		
HKACB56	1212	Production of IL-5	IL-5 FMAT. Assays for immunomodulatory proteins secreted by TH2 cells, mast cells, basophils, and	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-5

eosinophil function and B cell Ig production and promote polarization of CD4+ cells into	highly preferred embodiment of the invention includes a
Ig production and promote polarization of CD4+ cells into	of the invention includes a
polarization of CD4+ cells into	
	method for stimulating (e.g.,
TH2 cells are well known in	increasing) IL-5 production.
the art and may be used or	A highly preferred
routinely modified to assess	embodiment of the invention
the ability of polypeptides of	includes a method for
the invention (including	stimulating (e.g., increasing)
antibodies and agonists or	immunoglobulin production.
antagonists of the invention) to	An alternative highly preferred
mediate immunomodulation,	embodiment of the invention
stimulate immune cell	includes a method for
function, modulate B cell Ig	inhibiting (e.g., decreasing)
production, modulate immune	immunoglobulin production.
cell polarization, and/or	A highly preferred indication
mediate humoral or cell-	includes allergy. A highly
mediated immunity.	preferred indication includes
Exemplary assays that test for	asthma. A highly preferred
immunomodulatory proteins	indication includes rhinitis.
evaluate the production of	An additional highly preferred
cytokines, such as IL-5, and	indication is infection (e.g., an
the stimulation of eosinophil	infectious disease as described
function and B cell Ig	below under "Infectious
production. Such assays that	Disease"), and inflammation
may be used or routinely	and inflammatory disorders.
modified to test	Preferred indications include
immunomodulatory activity of	blood disorders (e.g., as
polypeptides of the invention	described below under
(including antibodies and	"Immune Activity", "Blood-
agonists or antagonists of the	Related Disorders", and/or
	antibodies and agonists or antagonists of the invention) to mediate immunomodulation, stimulate immune cell function, modulate B cell Ig production, modulate immune cell polarization, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as IL-5, and the stimulation of eosinophil function and B cell Ig production. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the

	invention) include the assays	"Cardiovascular Disorders").
	disclosed in Miraglia et al., J	Preferred indications include
	Biomolecular Screening 4:193-	autoimmune diseases (e.g.,
	204 (1999); Rowland et al.,	rheumatoid arthritis, systemic
	"Lymphocytes: a practical	lupus erythematosis, multiple
	approach" Chapter 6:138-160	sclerosis and/or as described
	(2000); Ohshima et al., Blood	below) and
	92(9):3338-3345 (1998); Jung	immunodeficiencies (e.g., as
	et al., Eur J Immunol	described below). Preferred
	25(8):2413-2416 (1995); Mori	indications include neoplastic
	et al., J Allergy Clin Immunol	diseases (e.g., leukemia,
	106(1 Pt 2):558-564 (2000);	lymphoma, melanoma, and/or
	and Koning et al., Cytokine	as described below under
	9(6):427-436 (1997), the	"Hyperproliferative
	contents of each of which are	Disorders"). Preferred
	herein incorporated by	indications include neoplasms
	reference in its entirety.	and cancers, such as, leukemia,
	Human T cells that may be	lymphoma, melanoma, and
	used according to these assays	prostate, breast, lung, colon,
	may be isolated using	pancreatic, esophageal,
 -	techniques disclosed herein or	stomach, brain, liver and
	otherwise known in the art.	urinary cancer. Other preferred
	Human T cells are primary	indications include benign
	human lymphocytes that	dysproliferative disorders and
 _	mature in the thymus and	pre-neoplastic conditions, such
	express a T cell receptor and	as, for example, hyperplasia,
	CD3, CD4, or CD8. These	metaplasia, and/or dysplasia.
	cells mediate humoral or cell-	Preferred indications include
	mediated immunity and may	anemia, pancytopenia,
	be preactivated to enhance	leukopenia, thrombocytopenia,
	responsiveness to	leukemias, Hodgkin's disease,

				immunomodulatory factors.	acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes
	HKACB56	1212	IFNg in Human T-		mellitus, endocarditis, meningitis, and Lyme Disease.
264			cell 2B9	22.5	
,	HKACB56	1212	Activation of	Kinase assay. JNK and p38	A highly preferred
264			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	sumulating endothelial cell
				apoptosis are well known in the art and may be used or	grown. An ancinative inginy preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
		_		antibodies and agonists or	embodiment of the invention
				antagonists of the invention) to	includes a method for
				proliferation activation and	stillinating circotherial cell
				apoptosis. Exemplary assays	highly preferred embodiment
				for JNK and p38 kinase	of the invention includes a

	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
,	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for
	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A

		involved in functions that	highly preferred embodiment
		include, but are not limited to,	of the invention includes a
,		angiogenesis, vascular	method for reducing cardiac
4		permeability, vascular tone,	hypertrophy. An alternative
		and immune cell extravasation.	highly preferred embodiment
			of the invention includes a
			method for inducing cardiac
			hypertrophy. Highly
			preferred indications include
			neoplastic diseases (e.g., as
			described below under
			"Hyperproliferative
			Disorders"), and disorders of
			the cardiovascular system
			(e.g., heart disease, congestive
			heart failure, hypertension,
			aortic stenosis,
			cardiomyopathy, valvular
			regurgitation, left ventricular
			dysfunction, atherosclerosis
			and atherosclerotic vascular
			disease, diabetic nephropathy,
			intracardiac shunt, cardiac
			hypertrophy, myocardial
			infarction, chronic
			hemodynamic overload, and/or
			as described below under
			"Cardiovascular Disorders").
			Highly preferred indications
			include cardiovascular,
			endothelial and/or angiogenic

			include cancers such as
			prostate breast ling colon
			prostate, oreast, rung, coron,
			pancreatic, esophageal,
			stomach, brain, liver, and
			urinary cancer. Preferred
			indications include benign
			dysproliferative disorders and
			pre-neoplastic conditions, such
			as, for example, hyperplasia,
			metaplasia, and/or dysplasia.
			Highly preferred indications
			also include arterial disease,
			such as, atherosclerosis,
			hypertension, coronary artery
			disease, inflammatory
			vasculitides, Reynaud"s
,			disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
			lymphedema; and other
			vascular disorders such as
			peripheral vascular disease,
	***		and cancer. Highly
			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from

	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.	Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic	and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders,	age-related inactual degeneration, and treatment /prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and	vascular disease. Preferred indications include blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders").
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autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	
	RANTES FMAT. Assays for immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediated immunity. Exemplary assays that test for
	Production of RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1212
	HKACB56
	264

immunomodulatory proteins evaluate the production of cytokines, such as RANTES,	chemotactic responses in immune cells. Such assays that may be used or routinely	modified to test immunomodulatory activity of	polypeptides of the invention (including antibodies and agonists or antagonists of the	invention) include the assays disclosed in Miraglia et al., J	Biomolecular Screening 4:193-204 (1999): Rowland et al.,	"Lymphocytes: a practical annroach" Chanter 6:138-160	(2000): Cocchi et al., Science 270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	(1995), the contents of each of	which are herein incorporated	by reference in its entirety. Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	Exemplary endothelial cells	that may be used according to
				·	,										

	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders", "Hyperproliferative Disorders" and/or "Cardiovascular Disorders"). Highly preferred indications include neoplasms and cancers such as, for example, leukemia, lymphoma,
these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expresssion in endothelial cells. Endothelial cells are cells that line blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation. Exemplary
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1212
	HKACB56
	264

			A	Transport of the Control of the Cont	
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
		-		endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
		•		expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for
_				upregulated by cytokines or	example, hyperplasia,
				other factors, and contributes	metaplasia, and/or dysplasia.
				to the extravasation of	
				lymphocytes, leucocytes and	
				other immune cells from blood	
				vessels; thus VCAM	
				expression plays a role in	
				promoting immune and	
				inflammatory responses.	
264	HKACB56	1212	SEAP in SW480		
	HKACD58	1213	Regulation of	Assays for the regulation of	A highly preferred indication
265			transcription via	transcription through the	is diabetes mellitus.
			DMEF1 response	DMEF1 response element are	Additional highly preferred
			element in	well-known in the art and may	indications include
			adipocytes and pre-	be used or routinely modified	complications associated with
			adipocytes	to assess the ability of	diabetes (e.g., diabetic
				polypeptides of the invention	retinopathy, diabetic
				(including antibodies and	nephropathy, kidney disease
				agonists or antagonists of the	(e.g., renal failure,
				invention) to activate the	nephropathy and/or other
				DMEF1 response element in a	diseases and disorders as

		reporter construct (such as that	described in the "Renal
		containing the GLUT4	Disorders" section below),
		promoter) and to regulate	diabetic neuropathy, nerve
		insulin production. The	disease and nerve damage
		DMEF1 response element is	(e.g., due to diabetic
		present in the GLUT4	neuropathy), blood vessel
		promoter and binds to MEF2	blockage, heart disease, stroke,
-		transcription factor and another	impotence (e.g., due to diabetic
		transcription factor that is	neuropathy or blood vessel
		required for insulin regulation	blockage), seizures, mental
		of Glut4 expression in skeletal	confusion, drowsiness,
		muscle. GLUT4 is the primary	nonketotic hyperglycemic-
		insulin-responsive glucose	hyperosmolar coma,
		transporter in fat and muscle	cardiovascular disease (e.g.,
		tissue. Exemplary assays that	heart disease, atherosclerosis,
		may be used or routinely	microvascular disease,
		modified to test for DMEF1	hypertension, stroke, and other
•		response element activity (in	diseases and disorders as
		adipocytes and pre-adipocytes)	described in the
		by polypeptides of the	"Cardiovascular Disorders"
		invention (including antibodies	section below), dyslipidemia,
		and agonists or antagonists of	endocrine disorders (as
		the invention) include assays	described in the "Endocrine
	-	disclosed inThai, M.V., et al., J	Disorders" section below),
		Biol Chem, 273(23):14285-92	neuropathy, vision impairment
		(1998); Mora, S., et al., J Biol	(e.g., diabetic retinopathy and
		Chem, 275(21):16323-8	blindness), ulcers and impaired
		(2000); Liu, M.L., et al., J Biol	wound healing, and infection
		Chem, 269(45):28514-21	(e.g., infectious diseases and
		(1994); "Identification of a 30-	disorders as described in the
		base pair regulatory element	"Infectious Diseases" section

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below, especially of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.																			
and novel DNA binding	protein that regulates the	human GLUT4 promoter in	transgenic mice", J Biol Chem.	2000 Aug 4;275(31):23666-73;	Berger, et al., Gene 66:1-10	(1988); and, Cullen, B., et al.,	Methods in Enzymol.	216:362–368 (1992), the	contents of each of which is	herein incorporated by	reference in its entirety.	Adipocytes and pre-adipocytes	that may be used according to	these assays are publicly	available (e.g., through the	ATCC) and/or may be	routinely generated.	Exemplary cells that may be	used according to these assays	include the mouse 3T3-L1 cell	line which is an adherent	mouse preadipocyte cell line.	Mouse 3T3-L1 cells are a	continuous substrain of 3T3	fibroblasts developed through	clonal isolation. These cells	undergo a pre-adipocyte to	adipose-like conversion under	appropriate differentiation	culture conditions.
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	HKACD58	1213	II -2 in Human T		
265			cells	-	
	HKACD58	1213	Activation of	Assays for the activation of	A preferred embodiment of
265			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
	•		response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
	***			the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
				66:1-10 (1998); Cullen and	immune response, and
				Malm, Methods in Enzymol	suppressing a T cell-mediated
				216:362-368 (1992); Henthorn	immune response. Additional
				et al., Proc Natl Acad Sci USA	highly preferred indications

include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia.
85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,	which is a human natural killer	cell line with cytolytic and	cytotoxic activity.														
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					Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease.")
265	HKACD58	1213	Caspase (+camptothecin) in SW480		
265	HKACD58	1213	Caspase (+paclitaxel) in SW480		
266	НКАСН44	1214	Activation of Endothelial Cell p38 or JNK Signaling Pathway.	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly

	the art and may be used or	preferred embodiment of the
	routinely modified to assess	invention includes a method
	the ability of polypeptides of	for inhibiting endothelial cell
	the invention (including	growth. A highly preferred
	antibodies and agonists or	embodiment of the invention
	antagonists of the invention) to	includes a method for
	promote or inhibit cell	stimulating endothelial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
-	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
-	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the

activation of and/or inactivating endothelial cells. A highly preferred embodiment of the invention includes a method for stimulating angiogenisis. An	\$	highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular
used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human	umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular	and immune cell extravasation.
		;

disease, diabetic nephropathy,	intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as. Kaposi"s sarcoma.
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hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as

immune cells (such	are well-known in the art and	inflammatory disorders.
as eosinophils).	may be used or routinely	Additional highly preferred
	modified to assess the ability	indications include immune
 - to-	of polypeptides of the	and hematopoietic disorders
*	invention (including antibodies	(e.g., as described below under
	and agonists or antagonists of	"Immune Activity", and
	the invention) to modulate	"Blood-Related Disorders"),
	gene expression (commonly	autoimmune diseases (e.g.,
	via STAT transcription factors)	rheumatoid arthritis, systemic
	involved in a wide variety of	lupus erythematosis, Crohn's
	cell functions. Exemplary	disease, multiple sclerosis
	assays for transcription	and/or as described below),
	through the GAS response	immunodeficiencies (e.g., as
	element that may be used or	described below), boosting an
 	routinely modified to test	eosinophil-mediated immune
	GAS-response element activity	response and, alternatively,
	of polypeptides of the	suppressing an eosinophil-
	invention (including antibodies	mediated immune response.
	and agonists or antagonists of	
	the invention) include assays	
	disclosed in Berger et al., Gene	
	66:1-10 (1998); Cullen and	
	Malm, Methods in Enzymol	
	216:362-368 (1992); Henthorn	
	et al., Proc Natl Acad Sci USA	
-	85:6342-6346 (1988);	
	Matikainen et al., Blood	
	93(6):1980-1991 (1999); and	
	Henttinen et al., J Immunol	
	155(10):4582-4587 (1995); the	
	contents of each of which are	

herein incorporated by reference in its entirety. Moreover, exemplary assays that may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to activate or inhibit activation of immune	cells include assays disclosed and/or cited in: Mayumi M.,	"EoL-1, a human eosinophilic cell line" Leuk Lymphoma:	Jun;7(3):243-50 (1992);	bnattacharya 5, "Granulocyte macrophage colony-	stimulating factor and	interleukin-5 activate STAT5 and induce CIS1 mRNA in	human peripheral blood	eosinophils" Am J Kespir Cell Mol Biol; Mar;24(3):312-6	(2001); and, Du J, et al.,	"Engagement of the CrkL	adapter in interferencing	Chem; Oct 20;275(42):33167-	75 (2000); the contents of each	of which are herein	incorporated by reference in its

	Highly preferred indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma (e.g., T cell lymphoma, non-Hodgkins lymphoma, non-Hodgkin's disease), melanoma, and prostate,
entirety. Exemplary cells that may be used according to these assays include eosinophils. Eosinophils are a type of immune cell important in the late stage of allergic reactions; they are recruited to tissues and mediate the inflammtory response of late stage allergic reaction. Increases in GAS mediated transcription in eosinophils is typically a result of STAT activation, normally a direct consequence of interleukin or other cytokine receptor stimulation (e.g. IL3, IL5 or GMCSF).	Assays for the activation of transcription through the Gamma Interferon Activation Site (GAS) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT transcription factors and modulate gene expression involved in a wide variety of
	Activation of transcription through GAS response element in immune cells (such as T-cells).
	1215
	HKACM93
	267

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative		autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as described below), boosting a T cell-mediated immune response, and	immune response. Additional preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral infection impared by the control of the cardiovascular disorders").
cell functions. Exemplary assays for transcription through the GAS response element that may be used or routinely modified to test	GAS-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays	disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Matikainen et al., Blood 93(6):1980-1991 (1999); and Henttinen et al. Immunol	155(10):4582-4587 (1995), the contents of each of which are herein incorporated by reference in its entirety. Exemplary human T cells, such as the MOLT4 cell line, that may be used according to these assays are publicly available (e.g., through the ATCC).

				and a plant of the state of	infections associated with
					chronic granulomatosus
					disease and malignant
					osteoporosis, and/or an
					infectious disease as described
					below under "Infectious
					Disease"). An additional
					preferred indication is
					idiopathic pulmonary fibrosis.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					acute lymphocytic anemia
					(ALL), plasmacytomas,
					multiple myeloma, arthritis,
					AIDS, granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
	Page 18 Co.				diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
					asthma and allergy.
	HKACM93	1215	Activation of	Assays for the activation of	Highly preferred indications
267			transcription	transcription through the	include inflammation and
			through NFKB	NFKB response element are	inflammatory disorders.
			response element in	well-known in the art and may	Highly preferred indications
			immune cells (such	be used or routinely modified	include blood disorders (e.g.,

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as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below), and	immunodeficiencies (e.g., as	described below). An	additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,
to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to regulate NFKB	transcription factors and	modulate expression of	immunomodulatory genes.	Exemplary assays for	transcription through the	NFKB response element that	may be used or rountinely	modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Exemplary human T cells,
as T-cells).	·	***************************************	-							-										-			•							

,				such as the MOLT4, that may be used according to these assays are publicly available (e.g., through the ATCC).	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
268	HKAEL80	1216	Activation of Natural Killer Cell ERK Signaling Pathway.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely	A highly preferred embodiment of the invention includes a method for stimulating natural killer cell proliferation. An alternative highly preferred embodiment of the invention includes a

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method for inhibiting natural	killer cell proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating natural	killer cell differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting natural killer cell	differentiation. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under		infections (e.g., as described	below under "Infectious		indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	Disorders", and/or
modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Kyriakis JM,	Biochem Soc Symp 64:29-48	(1999); Chang and Karin,	Nature 410(6824):37-40	(2001); and Cobb MH, Prog	Biophys Mol Biol 71(3-4):479-	500 (1999); the contents of	each of which are herein	incorporated by reference in its	entirety. Natural killer cells	that may be used according to	these assays are publicly	available (e.g., through the	ATCC). Exemplary natural
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"Cardiovascular Disorders"). Highly preferred indications	include autoimmune diseases	systemic lupus erythematosis,	multiple sclerosis and/or as	described below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer,	lymphoma and leukemias.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma.
killer cells that may be used according to these assays	include the human natural killer cell lines (for example	NK-YT cells which have	cytolytic and cytotoxic	activity) or primary NK cells.																								
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						· · · · ·																						

					AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues,
					endocarditis, meningitis, Lyme Disease, and allergies.
	HKAEV06	1217	Regulation of viability and	Assays for the regulation of viability and proliferation of	A highly preferred indication is disperse mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
			,	the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test regulation of viability and	nonketotic hyperglycemic-
				proliferation of pancreatic beta	hyperosmolar coma,
\neg				cells by polypeptides of the	cardiovascular disease (e.g.,

	hypertension, stroke, and other diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, and infection	(e.g., infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional highly	preferred indications are	complications associated with	insulin resistance.
invention (including antibodies and agonists or antagonists of	the invention) include assays disclosed in: Ohtani KI, et al.,	Endocrinology, 139(1):172-8	(1998); Krautheim A, et al,	Exp Clin Endocrinol Diabetes,	107 (1):29-34 (1999), the	contents of each of which is	herein incorporated by	reference in its entirety.	Pancreatic cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary pancreatic cells that	may be used according to these	assays include HITT15 Cells.	HITT15 are an adherent	epithelial cell line established	from Syrian hamster islet cells	transformed with SV40. These	cells express glucagon,	somatostatin, and	glucocorticoid receptors. The	cells secrete insulin, which is	stimulated by glucose and	glucagon and suppressed by	somatostatin or	glucocorticoids. ATTC# CRL- insulin resistance.
		-				-								3-F-03		i.	•											

1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.			Assays for activation of	transcription are well-known in	the art and may be used and	routinely modified to assess	ability of polypeptides of the	invention to inhibit or activate	transcription. An example of	such an assay follows: Cells	were pretreated with SID	supernatants or controls for 15-	18 hours. SEAP activity was	measured after 48 hours.	LS174T is an epithelial colon	adenocarcinoma cell line. Its	tumourigenicity in nude mice	make cell line LS174T a model	for studies on the mechanism	of synthesis and secretion of	specific tumoral markers in	colon cancer. See, Patan et al.,	Circ Res, 89(8):732-39 (2001),	the contents of which are
	DT-ATP in DT-ATP-SW480	Insulin Inhibition in H4IIE	Activation of	Transcription																				
,	1217	1217	1217												*********	-		2477						*
	HKAEV06	HKAEV06	HKAEV06																					
	269	269		269																				

þ	ety.	tion of Preferred indications	the AP1 include neoplastic diseases				(e.g., as described below under				ite growth Disorders"), and infection		100						antibodies sclerosis and/or as described	conists of below) and	e assays immunodeficiencies (e.g., as	t al., Gene described below). Additional	en and highly preferred indications		Henthorn inflammatory disorders.	1 Sci USA Highly preferred indications		l Chem diseases (e.g., leukemia,		
herein incorporated by	reference in its entirety.	Assays for the activation of	transcription through the AP1	response element are well-	ent in known in the art and may be	(such used or routinely modified to	assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to modulate growth	and other cell functions.	Exemplary assays for	transcription through the AP1	response element that may be	used or routinely modified to	test AP1-response element	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	1.41 01.34 1.41
		Activation of	transcription	through AP1	response element in	immune cells (such	as T-cells).															**************************************					****			
	1	HKAEV06 1																						-						
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				18(9):4986-4993 (1998); and	"Hyperproliferative
_				Fraser et al., Eur J Immunol	Disorders"). Highly preferred
				29(3):838-844 (1999), the	indications include neoplasms
				contents of each of which are	and cancers, such as, leukemia,
				herein incorporated by	lymphoma, prostate, breast,
	-			reference in its entirety.	lung, colon, pancreatic,
				Human T cells that may be	esophageal, stomach, brain,
,				used according to these assays	liver, and urinary cancer. Other
				are publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
··-				responsive suspension-culture	Preferred indications include
			-	cell line.	arthritis, asthma, AIDS,
					allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
		·			plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
		,			inflammatory bowel disease,
					sepsis, psoriasis, suppression of
					immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
i c	HKAFK41	1218	Production of	Assays for measuring	Preferred embodiments of the
7/0			ICAM-1	expression of ICAM-1 are	invention include using

polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in	detection, diagnosis, prevention, and/or treatment of Vascular Disease,	Atherosclerosis, Restenosis, Stroke, and Asthma.						•••														
>	polypeptides of the invention deta (including antibodies and pre- agonists or antagonists of the Vas	- s	that may be used or routinely modified to measure ICAM-1	expression include assays disclosed in: Rolfe BF, et al.	Atherosclerosis, 149(1):99-110	(2000); Panettieri RA Jr, et al.,	(1995); and, Grunstein MM, et	al., Am J Physiol Lung Cell	Mol Physiol, 278(6):L1154-	L1163 (2000), the contents of	each of which is herein	incorporated by reference in its	entirety. Cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary cells that may be	used according to these assays	include Aortic Smooth Muscle	Cells (AOSMC); such as	bovine AOSMC.
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	HKAFK41	1218	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
270				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-6	includes a method for
				participates in IL-4 induced	stimulating (e.g., increasing)
				IgE production and increases	IL-6 production. An alternative
				IgA production (IgA plays a	highly preferred embodiment
				role in mucosal immunity).	of the invention includes a
				IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
				Deregulated expression of IL-6	reducing) IL-6 production. A
				has been linked to autoimmune	highly preferrred indication is
				disease, plasmacytomas,	the stimulation or enhancement
				myelomas, and chronic	of mucosal immunity. Highly
				hyperproliferative diseases.	preferred indications include
				Assays for immunomodulatory	blood disorders (e.g., as
				and differentiation factor	described below under
				proteins produced by a large	"Immune Activity", "Blood-
				variety of cells where the	Related Disorders", and/or
				expression level is strongly	"Cardiovascular Disorders"),
				regulated by cytokines, growth	and infection (e.g., as
				factors, and hormones are well	described below under
				known in the art and may be	"Infectious Disease"). Highly
				used or routinely modified to	preferred indications include
				assess the ability of	autoimmune diseases (e.g.,
				polypeptides of the invention	rheumatoid arthritis, systemic
				(including antibodies and	lupus erythematosis, multiple
_				agonists or antagonists of the	sclerosis and/or as described
				invention) to mediate	below) and
			~	immunomodulation and	immunodeficiencies (e.g., as
				differentiation and modulate T	described below). Highly
				cell proliferation and function.	preferred indications also
				Exemplary assays that test for	include boosting a B cell-

	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune
***	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders. Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
-	Human dendritic cells are	metaplasia, and/or dysplasia.

as 313-L1 cells)
as 313-L1 ce

	1219	antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on	present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its entirety.	Myoblast cell Assays for muscle cell Highly preferred indications proliferation are well known in include diabetes, myopathy, the art and may be used or muscle cell atrophy, cancers of
	1219	quantitation of the ATP	present which s present which s presence of met active cells. 3T mouse preadipc is a continuous 3T3 fibroblast of through clonal i were differentia adipose-like staused in the scre H and Meuth M 133 (1974), wh incorporated by entirety.	
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	antibodies and agonists or	cardiovascular disorders (such
	antagonists of the invention) to	as congestive heart failure,
	stimulate or inhibit myoblast	cachexia, myxomas, fibromas,
	cell proliferation. Exemplary	congenital cardiovascular
	assays for myoblast cell	abnormalities, heart disease,
	proliferation that may be used	cardiac arrest, heart valve
,	or routinely modified to test	disease, vascular disease, and
	activity of polypeptides and	also as described below under
	antibodies of the invention	"Cardiovascular Disorders"),
	(including agonists or	stimulating myoblast
	antagonists of the invention)	proliferation, and inhibiting
	include, for example, assays	myoblast proliferation.
	disclosed in: Soeta, C., et al.	
	"Possible role for the c-ski	
	gene in the proliferation of	
	myogenic cells in regenerating	
	skeletal muscles of rats" Dev	
	Growth Differ Apr;43(2):155-	
	64 (2001); Ewton DZ, et al.,	
	"IGF binding proteins-4, -5	
	and -6 may play specialized	
	roles during L6 myoblast	
	proliferation and	
	differentiation" J Endocrinol	
	Mar;144(3):539-53 (1995);	
	and, Pampusch MS, et	
	al.,"Effect of transforming	
	growth factor beta on	
 	proliferation of L6 and	
	embryonic porcine myogenic	
	cells" J Cell Physiol	

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel
Jun; 143(3):524-8 (1990); the contents of each of which are herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media.	Assays for measuring secretion of insulin are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate insulin secretion. For example, insulin secretion is measured by FMAT using anti-rat insulin antibodies. Insulin secretion from pancreatic beta cells is upregulated by glucose and also by certain
	Insulin Secretion
	1219
	HKAFT66
	271

proteins/peptides, and	blockage, heart disease, stroke,
disregulation is a key	impotence (e.g., due to diabetic
component in diabetes.	neuropathy or blood vessel
Exemplary assays that may be	blockage), seizures, mental
used or routinely modified to	confusion, drowsiness,
test for stimulation of insulin	nonketotic hyperglycemic-
secretion (from pancreatic	hyperosmolar coma,
 cells) by polypeptides of the	cardiovascular disease (e.g.,
invention (including antibodies	heart disease, atherosclerosis,
and agonists or antagonists of	microvascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Shimizu, H., et	diseases and disorders as
al., Endocr J, 47(3):261-9	described in the
 (2000); Salapatek, A.M., et al.,	"Cardiovascular Disorders"
Mol Endocrinol, 13(8):1305-	section below), dyslipidemia,
17 (1999); Filipsson, K., et al.,	endocrine disorders (as
Ann N Y Acad Sci, 865:441-4	described in the "Endocrine
(1998); Olson, L.K., et al., J	Disorders" section below),
Biol Chem, 271(28):16544-52	neuropathy, vision impairment
(1996); and, Miraglia S et. al.,	(e.g., diabetic retinopathy and
 Journal of Biomolecular	blindness), ulcers and impaired
Screening, 4:193-204 (1999),	wound healing, and infection
the contents of each of which	(e.g., infectious diseases and
is herein incorporated by	disorders as described in the
reference in its entirety.	"Infectious Diseases" section
Pancreatic cells that may be	below, especially of the
used according to these assays	urinary tract and skin), carpal
are publicly available (e.g.,	tunnel syndrome and
 through the ATCC) and/or	Dupuytren's contracture).
 may be routinely generated.	
Exemplary pancreatic cells that	indication is obesity and/or

				may be used according to these assays include HITT15 Cells. HITT15 are an adherent epithelial cell line established from Syrian hamster islet cells transformed with SV40. These cells express glucagon, somatostatin, and glucocorticoid receptors. The cells secrete insulin, which is stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-177 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78:	complications associated with obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.
271	HKAFT66	1219	Activation of transcription through GATA-3 response element in immune cells (such as mast cells).	This reporter assay measures activation of the GATA-3 signaling pathway in HMC-1 human mast cell line. Activation of GATA-3 in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the GATA3 response element are well-known in the art and may be used or	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammation and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under

	monney of the fitting of the second	"Imming A officity" "Dlood
	Tourney mounted to assess	minimic Activity, Diodu-
	the ability of polypeptides of	Related Disorders", and/or
	the invention (including	"Cardiovascular Disorders").
	antibodies and agonists or	Preferred indications include
	antagonists of the invention) to	autoimmune diseases (e.g.,
	regulate GATA3 transcription	rheumatoid arthritis, systemic
	factors and modulate	lupus erythematosis, multiple
	expression of mast cell genes	sclerosis and/or as described
	important for immune response	below) and
	development. Exemplary	immunodeficiencies (e.g., as
	assays for transcription	described below). Preferred
	through the GATA3 response	indications include neoplastic
	element that may be used or	diseases (e.g., leukemia,
	routinely modified to test	lymphoma, melanoma,
	GATA3-response element	prostate, breast, lung, colon,
	activity of polypeptides of the	pancreatic, esophageal,
	invention (including antibodies	stomach, brain, liver, and
	and agonists or antagonists of	urinary tract cancers and/or as
-	the invention) include assays	described below under
	disclosed in Berger et al., Gene	"Hyperproliferative
	66:1-10 (1998); Cullen and	Disorders"). Other preferred
	Malm, Methods in Enzymol	indications include benign
	216:362-368 (1992); Henthorn	dysproliferative disorders and
	et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
	Quant Biol 64:563-571 (1999);	Preferred indications include
	Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
	J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
	(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
	Cell 89(4):587-596 (1997); and acute lymphocytic anemia	acute lymphocytic anemia

				Henderson et al., Mol Cell Biol (ALL), plasmacytomas,	(ALL), plasmacytomas.
				14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
				contents of each of which are	lymphoma, arthritis, AIDS,
				herein incorporated by	granulomatous disease,
				reference in its entirety. Mast	inflammatory bowel disease,
				cells that may be used	sepsis, neutropenia,
				according to these assays are	neutrophilia, psoriasis,
				publicly available (e.g.,	suppression of immune
-				through the ATCC).	reactions to transplanted
				Exemplary human mast cells	organs and tissues, hemophilia,
				that may be used according to	hypercoagulation, diabetes
				these assays include the HMC-	mellitus, endocarditis,
				1 cell line, which is an	meningitis, and Lyme Disease.
				immature human mast cell line	
-				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
	HKAFT66	1219	Activation of	This reporter assay measures	Highly preferred indications
271			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
4				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under

		known in the art and may be	"Immune Activity". "Blood-
		used or routinely modified to	Related Disorders", and/or
		assess the ability of	"Cardiovascular Disorders").
		polypeptides of the invention	Preferred indications include
		(including antibodies and	autoimmune diseases (e.g.,
		agonists or antagonists of the	rheumatoid arthritis, systemic
		invention) to regulate NFAT	lupus erythematosis, multiple
		transcription factors and	sclerosis and/or as described
		modulate expression of genes	below) and
		involved in	immunodeficiencies (e.g., as
***		immunomodulatory functions.	described below). Preferred
		Exemplary assays for	indications include neoplastic
		transcription through the	diseases (e.g., leukemia,
		NFAT response element that	lymphoma, melanoma,
	non-karm-	may be used or routinely	prostate, breast, lung, colon,
	•	modified to test NFAT-	pancreatic, esophageal,
		response element activity of	stomach, brain, liver, and
		polypeptides of the invention	urinary tract cancers and/or as
		(including antibodies and	described below under
		agonists or antagonists of the	"Hyperproliferative
		invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia

				Hutchinson and McCloskey, J	(ALL), plasmacytomas,
				Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
				16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
				al., J Exp Med 188:527-537	granulomatous disease,
				(1998), the contents of each of	inflammatory bowel disease,
				which are herein incorporated	sepsis, neutropenia,
				by reference in its entirety.	neutrophilia, psoriasis,
				Mast cells that may be used	suppression of immune
				according to these assays are	reactions to transplanted
				publicly available (e.g.,	organs and tissues, hemophilia,
				through the ATCC).	hypercoagulation, diabetes
				Exemplary human mast cells	mellitus, endocarditis,
				that may be used according to	meningitis, and Lyme Disease.
				these assays include the HMC-	
				1 cell line, which is an	
				immature human mast cell line	
				established from the peripheral	
				blood of a patient with mast	
				cell leukemia, and exhibits	
				many characteristics of	
				immature mast cells.	
271	HKAFT66	1219	IFNg in Human T-cell 2B9		
	HKAFT66	1219	IL-10 in Human T-		
271			cell 2B9		
	HKAFT66	1219	SEAP in Jurkat/IL4		
271			promoter		
	HKAFT66	1219	SEAP in Jurkat/IL4		
271			promoter (antiCD3		
			co-stim)	Table 1	
	HKDBF34	1220	SEAP in 293/ISRE		

7117	000	TG : GT A TG		
HKDBF34	1220	DI-AIP in DI- ATP-SW480		
HKDBF34	1220	SEAP in HepG2/Squale- synthetase(stimulati on)	-	
HKDBF34	1220	Activation of transcription through NFKB response element in immune cells (such as T-cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that may be used or rountinely modified to test NFKB-response element activity of polypeptides of the invention (including antibodies and	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as described below). An additional highly preferred indication is infection (e.g., AIDS, and/or an infectious disease as described below
				Highly preferred indications
			disclosed in Berger et al., Gene	include neoplastic diseases

	66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
	Malm, Methods in Enzymol	lymphoma, and/or as described
	216:362-368 (1992); Henthorn	below under
	et al., Proc Natl Acad Sci USA	"Hyperproliferative
	85:6342-6346 (1988); Black et	Disorders"). Highly preferred
	al., Virus Gnes 15(2):105-117	indications include neoplasms
	(1997); and Fraser et al.,	and cancers, such as, for
 	29(3):838-844 (1999), the	example, melanoma, renal cell
	contents of each of which are	carcinoma, leukemia,
	herein incorporated by	lymphoma, and prostate,
	reference in its entirety.	breast, lung, colon, pancreatic,
	Exemplary human T cells,	esophageal, stomach, brain,
	such as the MOLT4, that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
 	assays are publicly available	benign dysproliferative
	 (e.g., through the ATCC).	disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications also
		include anemia, pancytopenia,
		leukopenia, thrombocytopenia,
		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
 		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
 _		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, sepsis, neutropenia,
		neutrophilia, psoriasis,
		hemophilia, hypercoagulation,

diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted organs, asthma and allergy.			A highly preferred embodiment of the invention	includes a metilou loi stimulating natural killer cell	proliferation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting natural	killer cell proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating natural	killer cell differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting natural killer cell	differentiation. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative
			assays, kinase	assay, for EKK signal transduction that regulate cell			may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the
	IL-8 in SW480	SEAP in ATP-3T3- L1	Activation of Natural Killer Cell	EKK Signaling Pathway																		
	1220	1221	1221																		_	
	HKDBF34	HKGAT94	HKGAT94																			
	272	273	273																			

		assavs disclosed in Forrer et	Disorders"), blood disorders
		al., Biol Chem 379(8-9):1101-	(e.g., as described below under
		1110 (1998); Kyriakis JM,	"Immune Activity",
		Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
		(1999); Chang and Karin,	and/or "Blood-Related
		Nature 410(6824):37-40	Disorders"), immune disorders
		(2001); and Cobb MH, Prog	(e.g., as described below under
		Biophys Mol Biol 71(3-4):479-	"Immune Activity") and
		500 (1999); the contents of	infections (e.g., as described
		each of which are herein	below under "Infectious
		incorporated by reference in its	Disease"). Preferred
		entirety. Natural killer cells	indications include blood
		that may be used according to	disorders (e.g., as described
		these assays are publicly	below under "Immune
		available (e.g., through the	Activity", "Blood-Related
		ATCC). Exemplary natural	Disorders", and/or
		killer cells that may be used	"Cardiovascular Disorders").
		according to these assays	Highly preferred indications
		include the human natural	include autoimmune diseases
		killer cell lines (for example,	(e.g., rheumatoid arthritis,
		NK-YT cells which have	systemic lupus erythematosis,
		cytolytic and cytotoxic	multiple sclerosis and/or as
		activity) or primary NK cells.	described below) and
			immunodeficiencies (e.g., as
			described below). Additional
	****		highly preferred indications
,,			include inflammation and
			inflammatory disorders.
			Highly preferred indications
			also include cancers such as,
			kidney, melanoma, prostate,

breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, urinary cancer, lymphoma and leukemias. Other preferred indications include benign dysproliferative disorders and pre-neoplastic	conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Other highly preferred indications include, pancytopenia, leukopenia, leukemias, Hodgkin's disease, acute lymphocytic anemia	(ALL), arthritis, asthma, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, immune reactions to transplanted organs and tissues, endocarditis, meningitis, Lyme Disease, and allergies.	A highly preferred embodiment of the invention includes a method for stimulating the production of GM-CSF. An alternative highly preferred embodiment of the invention includes a method for inhibiting the
			GM-CSF FMAT. GM-CSF is expressed by activated T cells, macrophages, endothelial cells, and fibroblasts. GM-CSF regulates differentiation and proliferation of granulocytesmacrophage progenitors and enhances antimicrobial activity
			Production of GM-CSF
			1222
7.647			HKGCO27
			274

in neutrophils, monocytes and	production of GM-CSF.
macrophage. Additionally,	Highly preferred indications
GM-CSF plays an important	include inflammation and
 role in the differentiation of	inflammatory disorders. An
dendritic cells and monocytes,	additional highly preferred
and increases antigen	indication is infection (e.g., as
presentation. GM-CSF is	described below under
considered to be a	"Infectious Disease".
proinflammatory cytokine.	Highly preferred indications
 Assays for immunomodulatory	include blood disorders (e.g.,
proteins that promote the	neutropenia (and the
production of GM-CSF are	prevention of neutropenia
well known in the art and may	(e.g., in HIV infected patients),
be used or routinely modified	and/or as described below
to assess the ability of	under "Immune Activity",
polypeptides of the invention	"Blood-Related Disorders",
(including antibodies and	and/or "Cardiovascular
agonists or antagonists of the	Disorders"). Highly preferred
invention) to mediate	indications also include
immunomodulation and	autoimmune diseases (e.g.,
modulate the growth and	rheumatoid arthritis, systemic
differentiation of leukocytes.	lupus erythematosis, multiple
Exemplary assays that test for	sclerosis and/or as described
immunomodulatory proteins	below) and
evaluate the production of	immunodeficiencies (e.g., as
 cytokines, such as GM-CSF,	described below). Additional
and the activation of T cells.	highly preferred indications
Such assays that may be used	include asthma. Highly
or routinely modified to test	preferred indications include
immunomodulatory activity of	neoplastic diseases (e.g.,
polypeptides of the invention	leukemia (e.g., acute

lymphoblastic leukemia, and acute myelogenous leukemia), lymphoma (e.g., non-	Hodgkin"s lymphoma and Hodgkin"s disease), and/or as described below under	"Hyperproliferative Disorders"). Highly preferred indications include neoplasms	and cancers, such as, leukemia, lymphoma, melanoma, and prostate, breast, lung, colon,	pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia,	metaplasia, and/or dysplasia. Highly preferred indications		transplanted organs and tissues	(e.g., bone marrow transplant);	accelerating myeloid recovery; and mobilizing hematopoietic	progenitor cells. Preferred	indications include boosting a	T cell-mediated immune	response, and alternatively,
(including antibodies and agonists or antagonists of the invention) include the assays	disclosed in Miraglia et al., J Biomolecular Screening 4:193- 204 (1999); Rowland et al.,	"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); and Ye et al., J Leukoc	Biol (58(2):225-255, the contents of each of which are herein incorporated by	reference in its entirety. Natural killer cells that may be	used according to these assays are publicly available (e.g.,	through the ATCC) or may be	isolated using techniques disclosed herein or otherwise	known in the art. Natural killer (NK) cells are large	granular lymphocytes that have	antigen. NK cells show	antibody-independent killing	of tumor cells and also recognize antibody bound on	target cells, via NK Fc	receptors, leading to cell-	mediated cytotoxicity.	

HKISB57	1223	Activation of JNK Signaling Pathway	Kinase assay. JNK kinase assays for signal transduction	suppressing a r cell-mediated immune response. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, and allergy. Highly preferred indications include asthma, allergy,
			that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK kinase activity that may be	hypersensitivity reactions, inflammation, and inflammatory disorders. Additional highly preferred indications include immune and hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s disease, multiple sclerosis

		2:	
		used or routinely modified to	and/or as described below),
		test JNK kinase-induced	immunodeficiencies (e.g., as
		activity of polypeptides of the	described below). Highly
		invention (including antibodies	preferred indications also
		and agonists or antagonists of	include boosting or inhibiting
		the invention) include the	immune cell proliferation.
		assays disclosed in Forrer et	Preferred indications include
		al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
		1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
		Cell Res 247(2): 495-504	described below under
		(1999); Kyriakis JM, Biochem	"Hyperproliferative
		Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
		Chang and Karin, Nature	indications include boosting an
		410(6824):37-40 (2001); and	eosinophil-mediated immune
		Cobb MH, Prog Biophys Mol	response, and suppressing an
		Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
		the contents of each of which	response.
		are herein incorporated by	
		reference in its entirety.	
		Exemplary cells that may be	
		used according to these assays	
		include eosinophils.	
		Eosinophils are important in	
		the late stage of allergic	
		reactions; they are recruited to	
		tissues and mediate the	
		inflammatory response of late	
		stage allergic reaction.	
ale annes		Moreover, exemplary assays	
		that may be used or routinely	
-		modified to assess the ability	

of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-
						-									,	,								•						

	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness, nonketotic hyperglycemic-hyperosmolar coma,
terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate transcription of Malic Enzyme, a key enzyme in lipogenesis. Malic enzyme is involved in lipogenesisand its expression is stimulted by insulin. ME promoter contains two direct repeat (DR1)- like elements MEp and MEd identified as putative PPAR response elements. ME promoter may also responds to AP1 and other transcription factors. Exemplary assays that may be used or routinely modified to
	Regulation of transcription of Malic Enzyme in adipocytes
	1223
	HKISB57
	275

	transcription of Malic Fuzvme	heart disease atherosclerosis
	(in adipoocytes) by	microvascular disease,
	polypeptides of the invention	hypertension, stroke, and other
	(including antibodies and	diseases and disorders as
	agonists or antagonists of the	described in the
	invention) include assays	"Cardiovascular Disorders"
	disclosed in: Streeper, R.S., et	section below), dyslipidemia,
	al., Mol Endocrinol,	endocrine disorders (as
	12(11):1778-91 (1998);	described in the "Endocrine
	Garcia-Jimenez, C., et al., Mol	Disorders" section below),
	Endocrinol, 8(10):1361-9	neuropathy, vision impairment
	(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
	Biol Chem, 274(25):17997-	blindness), ulcers and impaired
	8004 (1999); Ijpenberg, A., et	wound healing, and infection
-	al., J Biol Chem,	(e.g., infectious diseases and
	272(32):20108-20117 (1997);	disorders as described in the
	Berger, et al., Gene 66:1-10	"Infectious Diseases" section
	(1988); and, Cullen, B., et al.,	below, especially of the
	Methods in Enzymol.	urinary tract and skin), carpal
	216:362–368 (1992), the	tunnel syndrome and
	contents of each of which is	Dupuytren's contracture).
	herein incorporated by	An additional highly preferred
	reference in its entirety.	indication is obesity and/or
	Hepatocytes that may be used	complications associated with
	according to these assays are	obesity. Additional highly
	publicly available (e.g.,	preferred indications include
	through the ATCC) and/or	weight loss or alternatively,
	may be routinely generated.	weight gain. Aditional
	Exemplary hepatocytes that	highly preferred indications are
	may be used according to these	complications associated with
	assays includes the H4IIE rat	insulin resistance.

				liver hepatoma cell line.	
	HKMLK53	1224	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
276			Signaling Pathway	assays for signal transduction	include asthma, allergy,
	-1. *		in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
		***		invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
	-	P.v.		used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
	_,			the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
				Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
			-	Chang and Karin, Nature	indications include boosting an
				410(6824):37-40 (2001); and	eosinophil-mediated immune
				Cobb MH, Prog Biophys Mol	response, and suppressing an

eosinophil-mediated immune	response.																													
Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"

		Highly preferred indications include diabetes, myopathy, muscle cell atrophy, cancers of muscle (such as, rhabdomyoma, and rhabdosarcoma), cardiovascular disorders (such as congestive heart failure,
	Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation" J Allergy Clin Immunol; Sep;104(3 Pt 1):565-74 (1999); the contents of each of which are herein incorporated by reference in its entirety.	Assays for muscle cell proliferation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to
To go septiminal to the second se		Myoblast cell proliferation
		HKMLM11 1225
		277

cachexia, myxomas, fibromas.	congenital cardiovascular	abnormalities, heart disease,	cardiac arrest, heart valve	disease, vascular disease, and	also as described below under	"Cardiovascular Disorders"),	stimulating myoblast	proliferation, and inhibiting	myoblast proliferation.	•																				
t myoblast	Exemplary	st cell	nay be used	ied to test	tides and	nvention	s or	invention)	le, assays	, C., et al.	he c-ski	ration of	regenerating	frats" Dev	;43(2):155-	DZ, et al.,	ins-4, -5	ecialized	oblast		Endocrinol	; (1995);	i, et	forming	uo	and	myogenic	ol	1990); the	which are
stimulate or inhibit myoblast	cell proliferation. Exemplary	assays for myoblast cell	proliferation that may be used	or routinely modified to test	activity of polypeptides and	antibodies of the invention	(including agonists or	antagonists of the invention)	include, for example, assays	disclosed in: Soeta, C., et al.	"Possible role for the c-ski	gene in the proliferation of	myogenic cells in regenerating	skeletal muscles of rats" Dev	Growth Differ Apr;43(2):155-	64 (2001); Ewton DZ, et al.,	"IGF binding proteins-4, -5	and -6 may play specialized	roles during L6 myoblast	proliferation and	differentiation" J Endocrinol	Mar;144(3):539-53 (1995);	and, Pampusch MS, et	al.,"Effect of transforming	growth factor beta on	proliferation of L6 and	embryonic porcine myogenic	cells" J Cell Physiol	Jun;143(3):524-8 (1990); the	contents of each of which are
stimu	cell p	assay	prolii	or ro	activi	antib	(inclu	antag	inclu	discle	"Poss	gene	myog	skelet	Grow	64 (2)	"IGF	and -(roles	prolif	differ	Mar;1	and, F	al.,"E	growt	prolif	embry	cells"	Jun; 1,	conte
										•																				
										-																				
																														i
																		<u>.</u>							•		_			
																									-					
					-									147														_		

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications
herein incorporated by reference in their entirety. Exemplary myoblast cells that may be used according to these assays include the rat myoblast L6 cell line. Rat myoblast L6 cells are an adherent rat myoblast cell line, isolated from primary cultures of rat thigh muscle, that fuse to form multinucleated myotubes and striated fibers after culture in differentiation media	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or routinely modified to test SRE
	Activation of transcription through serum response element in immune cells (such as T-cells).
	1226
	HKMLP68
	8 27 27

		:	
		the invention (including	(e.g., rheumatoid arthritis,
		antibodies and agonists or	systemic lupus erythematosis,
		antagonists of the invention)	Crohn"s disease, multiple
		include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
		12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
•		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
		line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,

HKMLP68 1226		1226		IL-2 in Human T-		
2/8 cell HKMMD13 1777 DECOM	1227		cell	cell 2B9		
1771	1771		End	Endothelial Cell	Caspase Apoptosis Rescue. Assays for caspase apoptosis	A highly preferred embodiment of the invention
Apor	Apor	Apor	Apor	Apoptosis.	rescue are well known in the	includes a method for
					art and may be used or	stimulating endothelial cell
					routinely modified to assess	growth. An alternative highly
					the ability of the polypeptides	preferred embodiment of the
					of the invention (including	invention includes a method
					antibodies and agonists or	for inhibiting endothelial cell
					antagonists of the invention) to	growth. A highly preferred
					inhibit caspase protease-	embodiment of the invention
					mediated apoptosis.	includes a method for
					Exemplary assays for caspase	stimulating endothelial cell
					apoptosis that may be used or	proliferation. An alternative
					routinely modified to test	highly preferred embodiment
	-				caspase apoptosis rescue of	of the invention includes a
					polypeptides of the invention	method for inhibiting
					(including antibodies and	endothelial cell proliferation.
					agonists or antagonists of the	A highly preferred
					invention) include the assays	embodiment of the invention
					disclosed in Romeo et al.,	includes a method for
					Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
				- 10.	(2000); Messmer et al., Br J	growth. An alternative highly
					Pharmacol 127(7): 1633-1640	preferred embodiment of the
					(1999); and J Atheroscler	invention includes a method
					Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
					the contents of each of which	growth. A highly preferred
	•				are herein incorporated by	
					reference in its entirety.	includes a method for
			ł		Endothelial cells that may be	stimulating apoptosis of

					
endothelial cells. An alternative highly preferred embodiment of the invention includes a method for	inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention includes a method for	stimulating angiogenisis. An alternative highly preferred embodiment of the invention includes a method for hibiting angiogenesis.	imer s a diac diac tive imer s a	method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disordered), and disordered of	the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,
used according to these assays are publicly available (e.g., through commercial sources).	that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example of endothelial cells which line	blood vessels and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability vascular tone	and immune cell extravasation.		

cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular	disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications	include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels	such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins	and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that	inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s

sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma,	hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign dysproliferative disorders and	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s

phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and	lymphedema; and other vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also	include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions).	implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis, cerebrovascular disease, renal diseases such as acute renal failure, and osteoporosis.	Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment
				-

					/prevention of endometriosis
	,				and related conditions.
					Additional highly preferred
	-				indications include fibromas,
					heart disease, cardiac arrest,
					heart valve disease, and
					vascular disease. Preferred
					indications include blood
					disorders (e.g., as described
					below under "Immune
-					Activity", "Blood-Related
					Disorders", and/or
	,				"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
)					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
279	HKMMD13	1227	Inhibition of squalene synthetase	Reporter Assay: construct contains regulatory and coding	

		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention
sequence of squalene synthetase, the first specific enzyme in the cholesterol biosynthetic pathway. See Jiang, et al., J. Biol. Chem. 268:12818-128241(993), the contents of which are herein incorporated by reference in its entirety. Cells were treated with SID supernatants, and SEAP activity was measured after 72 hours. HepG2 is a human hepatocellular carcinoma cell line (ATCC HB-8065). See Knowles et al., Science. 209:497-9 (1980), the contents of which are herein incorporated by reference in its entirety.		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or
gene transcription.	TNFa in Human T-cell 293T	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1228	1228
	HKMND01	HKMND01
1761	280	280

antago	antagonists of the invention) to	includer a method for
promo		stimulating endothelial cell
prolife	proliferation, activation, and	proliferation. An alternative
apopto	apoptosis. Exemplary assays	highly preferred embodiment
N. Join J. M. John J. M. J. M. John J. M. J. M. John J. M. J. M. John J. M. J	for JNK and p38 kinase	of the invention includes a
activity	activity that may be used or	method for inhibiting
routine	routinely modified to test JNK	endothelial cell proliferation.
and p3	and p38 kinase-induced	A highly preferred
activity	activity of polypeptides of the	embodiment of the invention
inventi	invention (including antibodies	includes a method for
and ag	and agonists or antagonists of	stimulating apoptosis of
the inv	the invention) include the	endothelial cells. An
assays	assays disclosed in Forrer et	alternative highly preferred
al., Bic	al., Biol Chem 379(8-9):1101-	embodiment of the invention
1110 (1110 (1998); Gupta et al., Exp	includes a method for
Cell Re	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
(6661)	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
Soc Sy	Soc Symp 64:29-48 (1999);	A highly preferred
Chang	Chang and Karin, Nature	embodiment of the invention
410(68	410(6824):37-40 (2001); and	includes a method for
Cobb N	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
Biol 71	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
the con	the contents of each of which	alternative highly preferred
are her)y	embodiment of the invention
referen		includes a method for
Endoth		inhibiting (e.g., decreasing) the
used ac	ays	activation of and/or
are pub	le (e.g.,	inactivating endothelial cells.
through		A highly preferred
Exemp		embodiment of the invention
that ma	that may be used according to	includes a method for

	these assays include human	stimulating angiogenisis. An
	umbilical vein endothelial cells	alternative highly preferred
 	(HUVEC), which are	embodiment of the invention
	endothelial cells which line	includes a method for
	venous blood vessels, and are	inhibiting angiogenesis. A
	involved in functions that	highly preferred embodiment
	include, but are not limited to,	of the invention includes a
	angiogenesis, vascular	method for reducing cardiac
	permeability, vascular tone,	hypertrophy. An alternative
	and immune cell extravasation.	highly preferred embodiment
		of the invention includes a
		method for inducing cardiac
		hypertrophy. Highly
		preferred indications include
		neoplastic diseases (e.g., as
		described below under
		"Hyperproliferative
		Disorders"), and disorders of
		the cardiovascular system
		(e.g., heart disease, congestive
		heart failure, hypertension,
		aortic stenosis,
		cardiomyopathy, valvular
		regurgitation, left ventricular
		dysfunction, atherosclerosis
		and atherosclerotic vascular
		disease, diabetic nephropathy,
 		intracardiac shunt, cardiac
		hypertrophy, myocardial
		infarction, chronic
-		hemodynamic overload, and/or

as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma.
		-																												
			-																	***										

angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	 peripheral Vascular disease.
					-									-	-					-									

preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as injury resulting from	balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury, rheumatoid arthritis,	diseases such as acute renal diseases such as acute renal failure, and osteoporosis. Additional highly preferred indications include stroke, graft rejection, diabetic or other retinopathies, thrombotic	and coagulative disorders, vascularitis, lymph angiogenesis, sexual disorders, age-related macular degeneration, and treatment /prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas, heart disease, cardiac arrest, heart valve disease, and vascular disease. Preferred indications include blood disorders (e.g., as

					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
280	HKMND01	1228	MCP-1 in HUVEC		
	HKMND01	1228	SEAP in OE-21		
280					
1	HKMND01	1228	SEAP in UMR-106		
280		i			
7	HL2AC08	1229	IL-2 in Human T-		
281			cell 293T		
	HL2AG57	1230	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred
282				by T cells and has strong	embodiment of the invention
				effects on B cells. IL-0	includes a method for

	participates in IL-4 induced	stimulating (e.g., increasing)
	IgE production and increases	IL-6 production. An alternative
	IgA production (IgA plays a	highly preferred embodiment
	role in mucosal immunity).	of the invention includes a
	IL-6 induces cytotoxic T cells.	method for inhibiting (e.g.,
	Deregulated expression of IL-6	reducing) IL-6 production. A
	has been linked to autoimmune	highly preferrred indication is
	disease, plasmacytomas,	the stimulation or enhancement
 -	myelomas, and chronic	of mucosal immunity. Highly
	hyperproliferative diseases.	preferred indications include
	Assays for immunomodulatory	blood disorders (e.g., as
	and differentiation factor	described below under
	proteins produced by a large	"Immune Activity", "Blood-
	variety of cells where the	Related Disorders", and/or
	expression level is strongly	"Cardiovascular Disorders"),
	regulated by cytokines, growth	and infection (e.g., as
	factors, and hormones are well	described below under
	known in the art and may be	"Infectious Disease"). Highly
	used or routinely modified to	preferred indications include
	assess the ability of	autoimmune diseases (e.g.,
	polypeptides of the invention	rheumatoid arthritis, systemic
	(including antibodies and	lupus erythematosis, multiple
	agonists or antagonists of the	sclerosis and/or as described
	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	evaluate the production of	and alternatively suppressing a
	cytokines, such as IL-6, and	B cell-mediated immune

	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may	urinary cancer. Other preferred
	be used according to these	indications include benign
	assays may be isolated using	dysproliferative disorders and
	techniques disclosed herein or	pre-neoplastic conditions, such
	otherwise known in the art.	as, for example, hyperplasia,
	Human dendritic cells are	metaplasia, and/or dysplasia.
	antigen presenting cells in	Preferred indications include
	suspension culture, which,	anemia, pancytopenia,
	when activated by antigen	leukopenia, thrombocytopenia,

			and functional activities.	rlodgkin s disease, acute lymphocytic anemia (ALL), multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease. An additonal preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
HLCND09 1231	1	DT-ATP in DT-ATP-SW480		
HLCND09 1231		SEAP in HIB/CRE		
HLCND09 1231		CD152 in Human T cells		
HLDBE54 1232	2	Protection from Endothelial Cell Apoptosis.	Caspase Apoptosis Rescue. Assays for caspase apoptosis rescue are well known in the art and may be used or routinely modified to assess	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the

of the invention (including	invention includes a method
 antibodies and agonists or	for inhihiting endothelial cell
antioones and agomes of	101 Hanotting chaotherial Cen
aniagonisis of the invention) to	growin. A nigniy preferred
inhibit caspase protease-	embodiment of the invention
mediated apoptosis.	includes a method for
 Exemplary assays for caspase	stimulating endothelial cell
apoptosis that may be used or	proliferation. An alternative
routinely modified to test	highly preferred embodiment
caspase apoptosis rescue of	of the invention includes a
polypeptides of the invention	method for inhibiting
 (including antibodies and	endothelial cell proliferation.
agonists or antagonists of the	A highly preferred
invention) include the assays	embodiment of the invention
disclosed in Romeo et al.,	includes a method for
Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
(2000); Messmer et al., Br J	growth. An alternative highly
 Pharmacol 127(7): 1633-1640	preferred embodiment of the
(1999); and J Atheroscler	invention includes a method
Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
the contents of each of which	growth. A highly preferred
are herein incorporated by	embodiment of the invention
reference in its entirety.	includes a method for
 Endothelial cells that may be	stimulating apoptosis of
used according to these assays	endothelial cells. An
are publicly available (e.g.,	alternative highly preferred
through commercial sources).	embodiment of the invention
Exemplary endothelial cells	includes a method for
 that may be used according to	inhibiting (e.g., decreasing)
these assays include bovine	apoptosis of endothelial cells.
aortic endothelial cells	A highly preferred
(bAEC), which are an example	embodiment of the invention

hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications	endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels	themselves, such as of the arteries, capillaries, veins and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly	preferred are indications that inhibit angiogenesis and/or cardiovascularization. Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s	sarcoma, and retinal disorders. Highly preferred indications include neoplasms and cancer, such as, Kaposi's sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis,
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hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,
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and cancer. Highly	preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease. Preferred	indications include blood
											-														\					
																											P-A-Miller			
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disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.		immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory immunomodulatory proteins from to f the invention and other cell types that exert a embodiment of the invention
		TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exer wide variety of inflammatory
	Caspase (+paclitaxel) in SW480	Production of TNF alpha by dendritic cells
	1232	1233
	HLDBE54	HLDBX13
	284	285

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includes a method for	Sumulating (e.g., increasing)	TNF alpha production.	Highly preferred indications	include blood disorders (e.g.,	as described below under	with "Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e a lentemia lymphoma
and cytotoxic effects on a	valiety of cells are well kilowii	in the art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to	mediate immunomodulation,	modulate inflammation and	cytotoxicity. Exemplary	assays that test for	immunomodulatory proteins	evaluate the production of	cytokines such as tumor	necrosis factor alpha (TNFa),	and the induction or inhibition	of an inflammatory or	cytotoxic response. Such	assays that may be used or	routinely modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204(1999); Rowland et al.,	"Lymphocytes: a practical	annroach" Chanter 6:138-160
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and/or as described below	under Hyperproliterative	Disorders). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, leukemia,	lymphoma, melanoma, glioma	(e.g., malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted
(2000); Verhasselt et al., Eur J	(1108): Dahlan et al. T	(1130), Dalliell et al., J	100(7):3585-3593	(1998); Verhasselt et al., J	Immunol 158:2919-2925	(1997); and Nardelli et al., J	Leukoc Biol 65:822-828	(1999), the contents of each of	which are herein incorporated	by reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.								
										***************************************					1	7.														
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organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention includes a method for
	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the invention (including antibodies and aconists or antagonists of
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1233
	HLDBX13
	285

	the invention) include the	endothelial cells. An
	 assays disclosed in Forrer et	alternative highly preferred
	 al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	 Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	 (1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	 Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	 Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	 are herein incorporated by	embodiment of the invention
	 reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
-	 used according to these assays	activation of and/or
	 are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	 Exemplary endothelial cells	embodiment of the invention
	 that may be used according to	includes a method for
	 these assays include human	stimulating angiogenisis. An
	 umbilical vein endothelial cells	alternative highly preferred
	 (HUVEC), which are	embodiment of the invention
	 endothelial cells which line	includes a method for
-	 venous blood vessels, and are	inhibiting angiogenesis. A
	 involved in functions that	highly preferred embodiment
	 include, but are not limited to,	of the invention includes a
	 angiogenesis, vascular	method for reducing cardiac
	 permeability, vascular tone,	hypertrophy. An alternative
	 and immune cell extravasation.	highly preferred embodiment
		of the invention includes a

hypetrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, a aortic stenosis, cardiomyopathy, valvular regurgitation, left venticular disease, diabetic nephropathy, intracardiae shunt, cardiae hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, emotohetial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels sthemselves, such as of the arteries, capillaries, veins				mosthood for industries
preferred indications include neoplastic diseases (e.g., sa described below under "Hyperpoliferative of the cardiovascular system (e.g., near disease, congestive hear failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, altherosclerosis and atherosclerosis and atherosclerosis and atherosclerosis and atherosclerosis intracardias shutt, cardiac hypertrophy, myocardial infraction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelia and/or aspicyemic disorders (e.g. systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				lifetiloa ioi iliaucilig calulac
perferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, andrie stensis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, andresselerosis and atheroselerosis hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as a described below under "Cardiovascular, endothetial andro angiogenic disorders (e.g., systemic disorders (e.g., systemic disorders that affect vessels such as diabetes of the vessels themselves, such as of the arteries, capillaries, veins				hypertrophy. Highly
described below under "Hyperpoliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stensois, cardiomyopathy, valvular regugitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiae shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothetial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				preferred indications include
described below under "Hyperpoliterative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dyskimction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardias shunt, cardiac hypertrophy, myocardial infraction, chronic hemodynamic overload, and/or as a described below under "Cardiovascular, enedothetial andor angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the eastels arteries, such as of the arteries, capillaries, veins				neoplastic diseases (e.g., as
"Hyperpoliferative Disorders"), and disorders of the cardiovascular system (e.g., heard disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atheroselerosis and atheroselerotic vascular disease, diabetic nephropathy, intracardiae shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				described below under
Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atheroselerosis and atheroselerosis and atheroselerotic vascular disease, diabetic nephropathy, intracardiae shunt, cardiae hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endotheital and/or angiogenic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				"Hyperproliferative
the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenois; cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerosis and atherosclerotic vascular intracardiae shunt, cardiae hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothetial and/or angiogenic disorders that affect vessels such as diseases of the vessels themselves, such as of the arteries, capillaries, veins				Disorders"), and disorders of
(e.g., heart disease, congestive heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				the cardiovascular system
heart failure, hypertension, aortic stenosis, cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerosic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"), Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				(e.g., heart disease, congestive
aortic stenosis, cardiomyopathy, valvular regugitation, left ventricular dysfunction, atherosclerosis and atherosclerosis and atherosclerosic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"), Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				heart failure, hypertension,
cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerosis and atherosclerotis vascular disease, diabetic nephropathy, intracardiae shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				aortic stenosis,
regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				cardiomyopathy, valvular
dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiae shunt, cardiae hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endotheital and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				regurgitation, left ventricular
and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				dysfunction, atherosclerosis
disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins	-	-		and atherosclerotic vascular
intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins		-		disease, diabetic nephropathy,
hypertrophy, myocardial infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins		-		intracardiac shunt, cardiac
infarction, chronic hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				hypertrophy, myocardial
hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				infarction, chronic
as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins			-	hemodynamic overload, and/or
"Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				as described below under
Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				"Cardiovascular Disorders").
include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				Highly preferred indications
endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				include cardiovascular,
disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				endothelial and/or angiogenic
disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				disorders (e.g., systemic
such as diabetes mellitus, as well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				disorders that affect vessels
well as diseases of the vessels themselves, such as of the arteries, capillaries, veins				such as diabetes mellitus, as
themselves, such as of the arteries, capillaries, veins				well as diseases of the vessels
arteries, capillaries, veins				themselves, such as of the
				arteries, capillaries, veins

and/or lymphatics). Highly preferred are indications that stimulate angiogenesis and/or cardiovascularization. Highly preferred are indications that inhibit angiogenesis and/or cardiovascularization.	Highly preferred indications include antiangiogenic activity to treat solid tumors, leukemias, and Kaposi"s sarcoma, and retinal disorders. Highly preferred indications include neonlasms and cancer	such as, Kaposi"s sarcoma, hemangioma (capillary and cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemangioendothelioma, angiosarcoma, haemangiopericytoma,	lymphangiosarcoma. Highly preferred indications also include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign

			dysproliferative disorders and
			pre-neoplastic conditions, such
			as, for example, hyperplasia,
			metaplasia, and/or dysplasia.
			Highly preferred indications
-			also include arterial disease,
-	-		such as, atherosclerosis,
			hypertension, coronary artery
			disease, inflammatory
			vasculitides, Reynaud"s
			disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
-			lymphedema; and other
			vascular disorders such as
		-	peripheral vascular disease,
			and cancer. Highly
			preferred indications also
			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
,,			balloon angioplasty, and
		-	atheroschlerotic lesions),
			implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
			cerebrovascular disease, renal

diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as
										-																				

described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.	o o	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly preferred embodiment of the invention includes a method
		Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced activity of polypeptides of the invention (including antibodies
	VEGF in SW480	Activation of Adipocyte ERK Signaling Pathway
	1233	1234
	HLDBX13	HLDNA86
	285	286

	to springer and springer of the	
	dir agomete or antagomete	
	me invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	
	Symp 64:29-48 (1999); Chang	
	and Karin, Nature	(e.g., as described below under
	410(6824):37-40 (2001); and	
	Cobb MH, Prog Biophys Mol	
	Biol 71(3-4):479-500 (1999);	
	the contents of each of which	
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
	include 3T3-L1 cells. 3T3-L1	
	is an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders
-	through clonal isolation and	(e.g., as described below under
	undergo a pre-adipocyte to	"Immine Activity") neural

disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as described below under	"Infectious Disease"). A highly preferred indication is diabetes mellitus.	additional nightly preferred indication is a complication associated with diabetes (e.g.,	diabetic retinopathy, diabetic nephropathy, kidney disease	(e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal	Disorders" section below), diabetic neuronathy nerve	disease and nerve damage	neuropathy), blood vessel	blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis
adipose-like conversion under appropriate differentiation conditions known in the art.															
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														-	
					1 d 1 d 1 d 1 d 1 d 1 d 1 d 1 d 1 d 1 d					-					

		microwscan lar disease
 	_	hence to attach
		nypertension, stroke, and other
 		diseases and disorders as
 	_	described in the
 		"Cardiovascular Disorders"
		section below), dyslipidemia,
		endocrine disorders (as
 		described in the "Endocrine
	_	Disorders" section below),
		neuropathy, vision impairment
		(e.g., diabetic retinopathy and
		blindness), ulcers and impaired
		wound healing, infection (e.g.,
 	-	infectious diseases and
		disorders as described in the
		"Infectious Diseases" section
		below (particularly of the
 -		urinary tract and skin). An
		additional highly preferred
		indication is obesity and/or
		complications associated with
 		obesity. Additional highly
 		preferred indications include
		r alte
		weight gain. Additional
		highly preferred indications are
		complications associated with
 		insulin resistance.
_		Additional highly preferred
		indications are disorders of the
		musculoskeletal systems

					including myopathies,
					muscular dystrophy, and/or as
					described herein.
					Additional highly preferred
					indications include,
					hypertension, coronary artery
		·			disease, dyslipidemia,
					gallstones, osteoarthritis,
					degenerative arthritis, eating
					disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
		•••			indications include neoplasms
					and cancer, such as,
					Iymphoma, leukemia and
	-				breast, colon, and kidney
					cancer. Additional preferred
					indications include melanoma,
					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
287	HLDON23	1235	Regulation of transcription	Assays for the regulation of transcription through the	A highly preferred indication is diabetes mellitus.
			namedia	ampant mandingmin	maiorina is alabered monitars.

	through the PEPCK	PEPCK promoter are well-	An additional highly preferred
	 promoter in	known in the art and may be	indication is a complication
	 hepatocytes	used or routinely modified to	associated with diabetes (e.g.,
		assess the ability of	diabetic retinopathy, diabetic
		polypeptides of the invention	nephropathy, kidney disease
		(including antibodies and	(e.g., renal failure,
	 	agonists or antagonists of the	nephropathy and/or other
	 	invention) to activate the	diseases and disorders as
		PEPCK promoter in a reporter	described in the "Renal
		construct and regulate liver	Disorders" section below),
		gluconeogenesis. Exemplary	diabetic neuropathy, nerve
		assays for regulation of	disease and nerve damage
	 	transcription through the	(e.g., due to diabetic
		PEPCK promoter that may be	neuropathy), blood vessel
		used or routinely modified to	blockage, heart disease, stroke,
1.77		test for PEPCK promoter	impotence (e.g., due to diabetic
		activity (in hepatocytes) of	neuropathy or blood vessel
		polypeptides of the invention	blockage), seizures, mental
		(including antibodies and	confusion, drowsiness,
		agonists or antagonists of the	nonketotic hyperglycemic-
		invention) include assays	hyperosmolar coma,
		disclosed in Berger et al., Gene	cardiovascular disease (e.g.,
		66:1-10 (1998); Cullen and	heart disease, atherosclerosis,
		Malm, Methods in Enzymol	microvascular disease,
		216:362-368 (1992); Henthorn	hypertension, stroke, and other
		et al., Proc Natl Acad Sci USA	diseases and disorders as
		85:6342-6346 (1988);	described in the
	-	Lochhead et al., Diabetes	"Cardiovascular Disorders"
		49(6):896-903 (2000); and	section below), dyslipidemia,
		Yeagley et al., J Biol Chem	endocrine disorders (as
		275(23):17814-17820 (2000),	described in the "Endocrine

Disorders" section below), neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	an infectious diseases or	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include glycogen	storage disease (e.g.,
the contents of each of which is herein incorporated by	reference in its entirety.	Hepatocyte cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC) and/or	may be routinely generated.	Exemplary liver hepatoma	cells that may be used	according to these assays	include H4lle cells, which	contain a tyrosine amino	transferase that is inducible	with glucocorticoids, insulin,	or cAMP derivatives.															
		1, 1																											
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glycogenoses), hepatitis,	gallstones, cirriosis of the	liver, degenerative or necrotic	liver disease, alcoholic liver	diseases, fibrosis, liver	regeneration, metabolic	disease, dyslipidemia and	cholesterol metabolism, and	hepatocarcinomas.	Highly preferred indications	include blood disorders (e.g.,	as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related	Disorders"), immune disorders	(e.g., as described below under	"Immune Activity"), infection	(e.g., an infectious disease	and/or disorder as described	below under "Infectious	Disease"), endocrine disorders	(e.g., as described below under	"Endocrine Disorders"), and	neural disorders (e.g., as	described below under "Neural	Activity and Neurological	Diseases").	Additional preferred	indications include neoplastic	diseases (e.g., as described
												-			-															
	-								<u>-</u>			-				-														

below under "Hyperproliferative Disorders"). Preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, and urinary cancer. A highly preferred indication is liver cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	Highly preferred indications include inflammation (acute and chronic), restnosis, atherosclerosis, asthma and allergy. Highly preferred indications include inflammation and inflammatory disorders, immunological disorders, neoplastic disorders (e.g. cancer/tumorigenesis), and cardiovascular disorders (such as described below under "Immune Activity", "Blood-Related Disorders",
below under "Hyperproliferative Disorders"). Preferred indications include neop and cancers, such as, let lymphoma, prostate, bre lung, colon, pancreatic, esophageal, stomach, br and urinary cancer. A hi preferred indication is li cancer. Other preferred indications include beni dysproliferative disorde pre-neoplastic condition as, for example, hyperpl metaplasia, and/or dysp	Highly preferred indicatic include inflammation (aca and chronic), restnosis, atherosclerosis, asthma ar allergy. Highly preferred inflammation and inflammatory disorders, immunological disorders (e.g. cancer/tumorigenesis), an cardiovascular disorders (as described below under "Immune Activity", "Blor Related Disorders",
	Assays for measuring expression of VCAM are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate VCAM expression. For example, FMAT may be used to meaure the upregulation of cell surface VCAM-1 expression in endothelial cells. Endothelial cells are cells that line blood
	Production of VCAM in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))
	1235
	HLDON23
	287

			vessels, and are involved in functions that include, but are	"Hyperproliferative Disorders" and/or "Cardiovascular
			not limited to, angiogenesis,	Disorders"). Highly preferred
			vascular permeability, vascular tone, and immune cell	indications include neoplasms and cancers such as, for
		-	extravasation. Exemplary	example, leukemia, lymphoma,
			endothelial cells that may be	melanoma, renal cell
			used according to these assays	carcinoma, and prostate,
			include human umbilical vein	breast, lung, colon, pancreatic,
			endothelial cells (HUVEC),	esophageal, stomach, brain,
			which are available from	liver and urinary cancer. Other
			commercial sources. The	preferred indications include
			expression of VCAM	benign dysproliferative
			(CD106), a membrane-	disorders and pre-neoplastic
			associated protein, can be	conditions, such as, for
	-		upregulated by cytokines or	example, hyperplasia,
			other factors, and contributes	metaplasia, and/or dysplasia.
			to the extravasation of	
			lymphocytes, leucocytes and	
		•	other immune cells from blood	
			vessels; thus VCAM	
			expression plays a role in	
			promoting immune and	
			inflammatory responses.	
1235	- P	ou of	Assays for measuring	Preferred embodiments of the
	<u> </u>	ICAM-1	expression of ICAM-1 are	invention include using
			well-known in the art and may	polypeptides of the invention
			be used or routinely modified	(or antibodies, agonists, or
			to assess the ability of	antagonists thereof) in
		<u>`</u>	polypeptides of the invention	detection, diagnosis,
	-		(including antibodies and	prevention, and/or treatment of

rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response.																					
inhibit production of IL-10	and/or activation of T-cells.	Exemplary assays that may be	used or routinely modified to	assess the ability of	polypeptides and antibodies of	the invention (including	agonists or antagonists of the	invention) to modulate IL-10	production and/or T-cell	proliferation include, for	example, assays such as	disclosed and/or cited in:	Robinson, DS, et al., "Th-2	cytokines in allergic disease"	Br Med Bull; 56 (4): 956-968	(2000), and Cohn, et al., "T-	helper type 2 cell-directed	therapy for asthma"	Pharmacology & Therapeutics;	88: 187-196 (2000); the	contents of each of which are	herein incorporated by	reference in their entirety.	Exemplary cells that may be	used according to these assays	include Th2 cells. IL10	secreted from Th2 cells may be	measured as a marker of Th2	cell activation. Th2 cells are	a class of T cells that secrete
										-			*.														_			

		Highly preferred indications	include allergy, asthma, and	rhinitis. Additional preferred	indications include infection	(e.g., an infectious disease as	described below under	"Infectious Disease"), and	inflammation and	inflammatory disorders.	Preferred indications also	include blood disorders (e.g.,	as described below under	"Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,
IL4, IL10, IL13, IL5 and IL6. Factors that induce differentiation and activation of Th2 cells play a major role in the initiation and pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.		This reporter assay measures	activation of the GATA-3	signaling pathway in HMC-1	human mast cell line.	Activation of GATA-3 in mast	cells has been linked to	cytokine and chemokine	production. Assays for the	activation of transcription	through the GATA3 response	element are well-known in the	art and may be used or	routinely modified to assess	the ability of polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention) to
	SEAP in HIB/CRE	Activation of	transcription	through GATA-3	response element in	immune cells (such	as mast cells).											
	1236	1236																
	HLDOW79	HLDOW79																
	288		288															

		regulate GATA3 transcription	rheumatoid arthritis, systemic
		factors and modulate	lupus erythematosis, multiple
	-	expression of mast cell genes	sclerosis and/or as described
		important for immune response	below) and
		development. Exemplary	immunodeficiencies (e.g., as
		assays for transcription	described below). Preferred
		through the GATA3 response	indications include neoplastic
		element that may be used or	diseases (e.g., leukemia,
-		routinely modified to test	lymphoma, melanoma,
		GATA3-response element	prostate, breast, lung, colon,
		activity of polypeptides of the	pancreatic, esophageal,
		invention (including antibodies	stomach, brain, liver, and
		and agonists or antagonists of	urinary tract cancers and/or as
-		the invention) include assays	described below under
		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
	-	85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
		et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,

				cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
288	HLDOW79	1236	Activation of transcription through NFAT response element in immune cells (such as mast cells).	This reporter assay measures activation of the NFAT signaling pathway in HMC-1 human mast cell line. Activation of NFAT in mast cells has been linked to cytokine and chemokine production. Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention fincluding antibodies and	Highly preferred indications include allergy, asthma, and rhinitis. Additional preferred indications include infection (e.g., an infectious disease as described below under "Infectious Disease"), and inflammatory disorders. Preferred indications also include blood disorders (e.g., as described below under "Imnune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Preferred indications include

		e e	agonists or antagonists of the	rheumatoid arthritis, systemic
		ii	invention) to regulate NFAT	lupus erythematosis, multiple
		tr	transcription factors and	sclerosis and/or as described
		ш	modulate expression of genes	below) and
		ii	involved in	immunodeficiencies (e.g., as
		<u>:</u>	immunomodulatory functions.	described below). Preferred
	-	Ш	Exemplary assays for	indications include neoplastic
			transcription through the	diseases (e.g., leukemia,
		<u>Z</u>	NFAT response element that	lymphoma, melanoma,
		u	may be used or routinely	prostate, breast, lung, colon,
		ш	modified to test NFAT-	pancreatic, esophageal,
			response element activity of	stomach, brain, liver, and
		Q.	polypeptides of the invention	urinary tract cancers and/or as
-		<u>;)</u>	(including antibodies and	described below under
		8	agonists or antagonists of the	"Hyperproliferative
_		i	invention) include assays	Disorders"). Other preferred
		Ъ	disclosed in Berger et al., Gene	indications include benign
		9	66:1-10 (1998); Cullen and	dysproliferative disorders and
			Malm, Methods in Enzymol	pre-neoplastic conditions, such
		2	216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		ē	et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
· <u></u> -		<u></u>	85:6342-6346 (1988); De Boer	Preferred indications include
		G	et al., Int J Biochem Cell Biol	anemia, pancytopenia,
			31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		ē	et al., J Immunol	leukemias, Hodgkin's disease,
			165(12):7215-7223 (2000);	acute lymphocytic anemia
			Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		<u>m</u>	Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
			16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		ল	al., J Exp Med 188:527-537	granulomatous disease,
			(1998), the contents of each of	inflammatory bowel disease,

sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, and Lyme Disease.	
which are herein incorporated by reference in its entirety. Mast cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary human mast cells that may be used according to these assays include the HMC-1 cell line, which is an immature human mast cell line established from the peripheral blood of a patient with mast cell leukemia, and exhibits many characteristics of immature mast cells.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1236
	HLDOW79
	288

			Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Transo Activity.")
Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP present which signals the present which signals the presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation. Cells were differentiated to an adipose-like state before being used in the screen. See Green H and Meuth M., Cell 3: 127-133 (1974), which is herein incorporated by reference in its	chargy.		Assays for the activation of transcription through the AP1 response element are well-known in the art and may be used or routinely modified to assess the ability of
	SEAP in Jurkat/IL4 promoter	SEAP in Jurkat/IL4 promoter (antiCD3 co-stim)	Activation of transcription through AP1 response element in immune cells (such as T-cells).
	1236	1236	1236
	HLDOW79	HLDOW79	HLDOW79
	288	288	288

	(including antibodies and	"Cardiovascular Disorders",
	agonists or antagonists of the	and/or "Blood-Related
	invention) to modulate growth	Disorders"), and infection
	and other cell functions.	(e.g., an infectious disease as
	Exemplary assays for	described below under
	transcription through the AP1	"Infectious Disease"). Highly
	response element that may be	preferred indications include
	used or routinely modified to	autoimmune diseases (e.g.,
	test AP1-response element	rheumatoid arthritis, systemic
	activity of polypeptides of the	lupus erythematosis, multiple
 	invention (including antibodies	sclerosis and/or as described
	and agonists or antagonists of	below) and
 	the invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety.	lung, colon, pancreatic,
 	Human T cells that may be	esophageal, stomach, brain,
	used according to these assays	liver, and urinary cancer. Other
	are publicly available (e.g.,	preferred indications include

			through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is an IL-2 and IL-4 responsive suspension-culture cell line.	benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include arthritis, asthma, AIDS, allergy, anemia, pancytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, granulomatous disease, inflammatory bowel disease, sepsis, psoriasis, suppression of immune reactions to transplanted organs and tissues, endocarditis,
HLDOW79	1236	Activation of transcription through CD28 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for

	Exe	-	activating T cells. An
	trar	×	alternative highly preferred
	resi	response element that may be	embodiment of the invention
	nse	used or routinely modified to	includes a method for
	test	test CD28-response element	inhibiting the activation of
	act	activity of polypeptides of the	and/or inactivating T cells.
	vni	invention (including antibodies	A highly preferred
****	anc	and agonists or antagonists of	embodiment of the invention
	the the	the invention) include assays	includes a method for
	dis	disclosed in Berger et al., Gene	stimulating (e.g., increasing)
	99	66:1-10 (1998); Cullen and	IL-2 production. An alternative
	Ma	Malm, Methods in Enzymol	highly preferred embodiment
	210	216:362-368 (1992); Henthorn	of the invention includes a
	ets	et al., Proc Natl Acad Sci USA	method for inhibiting (e.g.,
	85:	85:6342-6346 (1988);	reducing) IL-2 production.
	Mc	McGuire and Iacobelli, J	Additional highly preferred
	mI Im	Immunol 159(3):1319-1327	indications include
	(1)	(1997); Parra et al., J Immunol	inflammation and
	16	166(4):2437-2443 (2001); and	inflammatory disorders.
	Bu	Butscher et al., J Biol Chem	Highly preferred indications
	3(1	3(1):552-560 (1998), the	include autoimmune diseases
	00	contents of each of which are	(e.g., rheumatoid arthritis,
	he	herein incorporated by	systemic lupus erythematosis,
	ref	reference in its entirety. T	multiple sclerosis and/or as
	leo	cells that may be used	described below),
	acı	according to these assays are	immunodeficiencies (e.g., as
	nd	publicly available (e.g.,	described below), boosting a T
,	thr	through the ATCC).	cell-mediated immune
		Exemplary human T cells that	response, and suppressing a T
	m	may be used according to these	cell-mediated immune
	as	assays include the SUPT cell	response. Highly preferred

resi	culture of IL-2 and IL-4 responsive T cells.	diseases (e.g., melanoma, renal
resi	ponsive T cells.	and and and and and
		cell carcinoma, leukemia,
		lymphoma, and/or as described
		below under
		"Hyperproliferative
		Disorders"). Highly preferred
		indications include neoplasms
		and cancers, such as, for
		example, melanoma (e.g.,
		metastatic melanoma), renal
M		cell carcinoma (e.g., metastatic
		renal cell carcinoma),
		leukemia, lymphoma (e.g., T
		cell lymphoma), and prostate,
		breast, lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
	***	benign dysproliferative
		disorders and pre-neoplastic
		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		A highly preferred indication
		includes infection (e.g.,
		AIDS, tuberculosis, infections
		associated with granulomatous
		disease, and osteoporosis,
		and/or as described below
		under "Infectious Disease"). A

					highly preferred indication is
					AIDS. Additional highly
					preferred indications include
					suppression of immune
					reactions to transplanted
					organs and/or tissues, uveitis,
					psoriasis, and tropical spastic
				200	paraparesis. Preferred
					indications include blood
		-			disorders (e.g., as described
					below under "Immune
					Activity", "Blood-Related
					Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications also
90					include anemia, pancytopenia,
	-1-2-				leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
9	HLDOW79	1236	Activation of	Assays for the activation of	Highly preferred indications
788			transcription	transcription through the	include blood disorders (e.g.,

	through NFAT	Nuclear Factor of Activated T	as described below under
	response element in	cells (NFAT) response element	"Immune Activity", "Blood-
	immune cells (such	are well-known in the art and	Related Disorders", and/or
	as T-cells).	may be used or routinely	"Cardiovascular Disorders").
		modified to assess the ability	Highly preferred indications
	•	of polypeptides of the	include autoimmune diseases
		invention (including antibodies	(e.g., rheumatoid arthritis,
		and agonists or antagonists of	systemic lupus erythematosis,
		the invention) to regulate	multiple sclerosis and/or as
		NFAT transcription factors and	described below),
		modulate expression of genes	immunodeficiencies (e.g., as
•		involved in	described below), boosting a T
		immunomodulatory functions.	cell-mediated immune
		Exemplary assays for	response, and suppressing a T
		transcription through the	cell-mediated immune
		NFAT response element that	response. Additional highly
-		may be used or routinely	preferred indications include
		modified to test NFAT-	inflammation and
		response element activity of	inflammatory disorders. An
		polypeptides of the invention	additional highly preferred
		(including antibodies and	indication is infection (e.g., an
		agonists or antagonists of the	infectious disease as described
		invention) include assays	ar,
		disclosed in Berger et al., Gene	Disease"). Preferred
 		66:1-10 (1998); Cullen and	indications include neoplastic
 		Malm, Methods in Enzymol	diseases (e.g., leukemia,
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms

				et al., Int J Biochem Cell Biol	and cancers, such as, for
				31(10):1221-1236 (1999);	example, leukemia, lymphoma,
				Fraser et al., Eur J Immunol	and prostate, breast, lung,
				29(3):838-844 (1999); and	colon, pancreatic, esophageal,
				Yeseen et al., J Biol Chem	stomach, brain, liver and
				268(19):14285-14293 (1993),	urinary cancer. Other preferred
				the contents of each of which	indications include benign
				are herein incorporated by	dysproliferative disorders and
				reference in its entirety. T	pre-neoplastic conditions, such
				cells that may be used	as, for example, hyperplasia,
				according to these assays are	metaplasia, and/or dysplasia.
				publicly available (e.g.,	Preferred indications also
				through the ATCC).	include anemia, pancytopenia,
				Exemplary human T cells that	leukopenia, thrombocytopenia,
				may be used according to these	Hodgkin's disease, acute
				assays include the SUPT cell	lymphocytic anemia (ALL),
				line, which is a suspension	plasmacytomas, multiple
·				culture of IL-2 and IL-4	myeloma, Burkitt's lymphoma,
				responsive T cells.	arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					asthma and allergy.
	HLDOW79	1236	Activation of	Assays for the activation of	Highly preferred indications
288			transcription	transcription through the	include inflammation and

	through NFKB	NFKB response element are	inflammatory disorders.
	response element in	well-known in the art and may	Highly preferred indications
	immune cells (such	be used or routinely modified	include blood disorders (e.g.,
	as T-cells).	to assess the ability of	as described below under
		polypeptides of the invention	"Immune Activity", "Blood-
		(including antibodies and	Related Disorders", and/or
		agonists or antagonists of the	"Cardiovascular Disorders").
		invention) to regulate NFKB	Highly preferred indications
		transcription factors and	include autoimmune diseases
		modulate expression of	(e.g., rheumatoid arthritis,
		immunomodulatory genes.	systemic lupus erythematosis,
		Exemplary assays for	multiple sclerosis and/or as
-		transcription through the	described below), and
		NFKB response element that	immunodeficiencies (e.g., as
		may be used or rountinely	described below). An
		modified to test NFKB-	additional highly preferred
		response element activity of	indication is infection (e.g.,
		polypeptides of the invention	AIDS, and/or an infectious
		(including antibodies and	disease as described below
		agonists or antagonists of the	under "Infectious Disease").
		invention) include assays	Highly preferred indications
		disclosed in Berger et al., Gene	include neoplastic diseases
		66:1-10 (1998); Cullen and	(e.g., melanoma, leukemia,
		Malm, Methods in Enzymol	lymphoma, and/or as described
		216:362-368 (1992); Henthorn	below under
		et al., Proc Natl Acad Sci USA	"Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Gnes 15(2):105-117	indications include neoplasms
		(1997); and Fraser et al.,	and cancers, such
		29(3):838-844 (1999), the	as,melanoma, renal cell
		contents of each of which are	carcinoma, leukemia,

				herein incorporated by	lymphoma, and prostate,
				reference in its entirety. T	breast, lung, colon, pancreatic,
				cells that may be used	esophageal, stomach, brain,
				according to these assays are	liver and urinary cancer. Other
				publicly available (e.g.,	preferred indications include
				through the ATCC).	benign dysproliferative
-				Exemplary human T cells that	disorders and pre-neoplastic
				may be used according to these	conditions, such as, for
				assays include the SUPT cell	example, hyperplasia,
				line, which is a suspension	metaplasia, and/or dysplasia.
				culture of IL-2 and IL-4	Preferred indications also
				responsive T cells.	include anemia, pancytopenia,
					leukopenia, thrombocytopenia,
******					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					suppression of immune
					reactions to transplanted
					organs, asthma and allergy.
	HLDQC46	1237	Activation of	Assays for the activation of	A preferred embodiment of
289	-		transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,

		response element in	(SRF) are well-known in the	radioina) TME olabo
			out and man be used on	icaucing) iidi aipila
			alt allu Illay de used of	production. An alternative
		as 1-cells).	routinely modified to assess	preferred embodiment of the
		*	the ability of polypeptides of	invention includes a method
			the invention (including	for stimulating (e.g.,
	-		antibodies and agonists or	increasing) TNF alpha
			antagonists of the invention) to	production. Preferred
			regulate the serum response	indications include blood
			factors and modulate the	disorders (e.g., as described
			expression of genes involved	below under "Immune
			in growth. Exemplary assays	Activity", "Blood-Related
			for transcription through the	Disorders", and/or
			SRE that may be used or	"Cardiovascular Disorders"),
			routinely modified to test SRE	Highly preferred indications
			activity of the polypeptides of	include autoimmune diseases
			the invention (including	(e.g., rheumatoid arthritis,
			antibodies and agonists or	systemic lupus erythematosis,
		1 2 2 2	antagonists of the invention)	Crohn"s disease, multiple
			include assays disclosed in	sclerosis and/or as described
			Berger et al., Gene 66:1-10	below), immunodeficiencies
			(1998); Cullen and Malm,	(e.g., as described below),
-			Methods in Enzymol 216:362-	boosting a T cell-mediated
-			368 (1992); Henthorn et al.,	immune response, and
			Proc Natl Acad Sci USA	suppressing a T cell-mediated
			85:6342-6346 (1988); and	immune response. Additional
			Black et al., Virus Genes	highly preferred indications
			12(2):105-117 (1997), the	include inflammation and
			content of each of which are	inflammatory disorders, and
			herein incorporated by	treating joint damage in
			reference in its entirety. T	patients with rheumatoid
			cells that may be used	arthritis. An additional highly

preferred indication is sepsis.	ingling preferred mulcations include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis. AIDS, granulomatous
according to these assays are	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.																					
															- 180-												-		

			- Aller and the second		
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLDQR62	1238	Regulation of	Assays for the regulation of	A highly preferred indication
290			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
	٠			regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
				Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel

		of the ATP present which	blockage, heart disease, stroke,
 		signals the presence of	impotence (e.g., due to diabetic
		metabolically active cells.	neuropathy or blood vessel
 		Exemplary assays that may be	blockage), seizures, mental
		used or routinely modified to	confusion, drowsiness,
 		test regulation of viability and	nonketotic hyperglycemic-
		proliferation of pancreatic beta	hyperosmolar coma,
 		cells by polypeptides of the	cardiovascular disease (e.g.,
 		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Friedrichsen BN,	diseases and disorders as
	,	et al., Mol Endocrinol,	described in the
 		15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
 		MA, et al., Endocrinology,	section below), dyslipidemia,
		139(4):1494-9 (1998); Hugl	endocrine disorders (as
		SR, et al., J Biol Chem 1998	described in the "Endocrine
		Jul 10;273(28):17771-9	Disorders" section below),
		(1998), the contents of each of	neuropathy, vision impairment
		which is herein incorporated	(e.g., diabetic retinopathy and
 		by reference in its entirety.	blindness), ulcers and impaired
		Pancreatic cells that may be	wound healing, and infection
		used according to these assays	(e.g., infectious diseases and
		are publicly available (e.g.,	disorders as described in the
		through the ATCC) and/or	"Infectious Diseases" section
		may be routinely generated.	below, especially of the
		Exemplary pancreatic cells that	urinary tract and skin), carpal
		may be used according to these	tunnel syndrome and
		assays include rat INS-1 cells.	Dupuytren's contracture). An
		INS-1 cells are a semi-	additional highly preferred
		adherent cell line established	indication is obesity and/or

				from cells isolated from an X-ray induced rat transplantable	complications associated with obesity. Additional highly
				insulinoma. These cells retain	preferred indications include
				characteristics typical of native	weight loss or alternatively,
				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
			.,	secretion. References: Asfari	complications associated with
				et al. Endocrinology 1992	insulin resistance.
				130:167.	
	HLDQR62	1238	Activation of	Assays for the activation of	Preferred indications include
290			transcription	transcription through the	blood disorders (e.g., as
			through cAMP	cAMP response element are	described below under
	,		response element in	well-known in the art and may	"Immune Activity", "Blood-
			immune cells (such	be used or routinely modified	Related Disorders", and/or
			as T-cells).	to assess the ability of	"Cardiovascular Disorders"),
				polypeptides of the invention	and infection (e.g., an
				(including antibodies and	infectious disease as described
				agonists or antagonists of the	below under "Infectious
				invention) to increase cAMP	Disease"). Preferred
				and regulate CREB	indications include
				transcription factors, and	autoimmune diseases (e.g.,
				modulate expression of genes	rheumatoid arthritis, systemic
				involved in a wide variety of	lupus erythematosis, multiple
				cell functions. Exemplary	sclerosis and/or as described
				assays for transcription	below), immunodeficiencies
				through the cAMP response	(e.g., as described below),
				element that may be used or	boosting a T cell-mediated
				routinely modified to test	immune response, and
				cAMP-response element	suppressing a T cell-mediated
				activity of polypeptides of the	immune response. Additional
				invention (including antibodies	preferred indications include

		and agonists or antagonists of	inflammation and
		the invention) include assays	inflammatory disorders.
		disclosed in Berger et al., Gene	Highly preferred indications
		66:1-10 (1998); Cullen and	include neoplastic diseases
		Malm, Methods in Enzymol	(e.g., leukemia, lymphoma,
		216:362-368 (1992); Henthorn	and/or as described below
		et al., Proc Natl Acad Sci USA	under "Hyperproliferative
		85:6342-6346 (1988); Black et	Disorders"). Highly preferred
		al., Virus Genes 15(2):105-117	indications include neoplasms
		(1997); and Belkowski et al., J	and cancers, such as, for
		Immunol 161(2):659-665	example, leukemia, lymphoma
		(1998), the contents of each of	(e.g., T cell lymphoma,
		which are herein incorporated	Burkitt's lymphoma, non-
		by reference in its entirety. T	Hodgkins lymphoma,
		cells that may be used	Hodgkin"s disease),
		according to these assays are	melanoma, and prostate,
		publicly available (e.g.,	breast, lung, colon, pancreatic,
		through the ATCC).	esophageal, stomach, brain,
		Exemplary mouse T cells that	liver and urinary cancer. Other
	,	may be used according to these	preferred indications include
		assays include the CTLL cell	benign dysproliferative
		line, which is a suspension	disorders and pre-neoplastic
		culture of IL-2 dependent	conditions, such as, for
		cytotoxic T cells.	example, hyperplasia,
			metaplasia, and/or dysplasia.
			Preferred indications include
м	-		anemia, pancytopenia,
			leukopenia, thrombocytopenia,
			acute lymphocytic anemia
			(ALL), plasmacytomas,
			multiple myeloma, arthritis,

					AIDS, granulomatous disease,
					initianimatory bowei disease, sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
		-			reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease, and
- 1					asthma and allergy.
	HLDQU79	1239	Regulation of	Assays for the regulation of	A highly preferred indication
			viability and	viability and proliferation of	is diabetes mellitus. An
			proliferation of	cells in vitro are well-known in	additional highly preferred
			pancreatic beta	the art and may be used or	indication is a complication
			cells.	routinely modified to assess	associated with diabetes (e.g.,
				the ability of polypeptides of	diabetic retinopathy, diabetic
				the invention (including	nephropathy, kidney disease
				antibodies and agonists or	(e.g., renal failure,
				antagonists of the invention) to	nephropathy and/or other
				regulate viability and	diseases and disorders as
				proliferation of pancreatic beta	described in the "Renal
				cells. For example, the Cell	Disorders" section below),
			,	Titer-Glo luminescent cell	diabetic neuropathy, nerve
				viability assay measures the	disease and nerve damage
				number of viable cells in	(e.g., due to diabetic
				culture based on quantitation	neuropathy), blood vessel
				of the ATP present which	blockage, heart disease, stroke,
				signals the presence of	impotence (e.g., due to diabetic
				metabolically active cells.	neuropathy or blood vessel
- 1				Exemplary assays that may be	blockage), seizures, mental

	used or routinely modified to	confusion, drowsiness.
	test regulation of viability and	nonketotic hyperglycemic-
-	proliferation of pancreatic beta	hyperosmolar coma,
	cells by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Friedrichsen BN,	diseases and disorders as
	et al., Mol Endocrinol,	described in the
	15(1):136-48 (2001); Huotari	"Cardiovascular Disorders"
	MA, et al., Endocrinology,	section below), dyslipidemia,
	139(4):1494-9 (1998); Hugl	endocrine disorders (as
	SR, et al., J Biol Chem 1998	described in the "Endocrine
	Jul 10;273(28):17771-9	Disorders" section below),
	(1998), the contents of each of	neuropathy, vision impairment
	which is herein incorporated	(e.g., diabetic retinopathy and
	by reference in its entirety.	blindness), ulcers and impaired
	Pancreatic cells that may be	wound healing, and infection
	used according to these assays	(e.g., infectious diseases and
	are publicly available (e.g.,	disorders as described in the
	through the ATCC) and/or	"Infectious Diseases" section
	may be routinely generated.	below, especially of the
	Exemplary pancreatic cells that	urinary tract and skin), carpal
	may be used according to these	tunnel syndrome and
	assays include rat INS-1 cells.	Dupuytren's contracture). An
	INS-1 cells are a semi-	additional highly preferred
	adherent cell line established	indication is obesity and/or
	from cells isolated from an X-	complications associated with
	ray induced rat transplantable	obesity. Additional highly
	insulinoma. These cells retain	preferred indications include
	characteristics typical of native	weight loss or alternatively,

				pancreatic beta cells including	weight gain. Additional highly
				glucose inducible insulin	preferred indications are
				secretion. References: Asian	complications associated with
(**184				et al. Endocrinology 1992 130:167.	insulin resistance.
	нгроп79	1239	Activation of	Assays for the activation of	A preferred embodiment of
291			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
	_			antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
	~			activity of the polypeptides of	include autoimmune diseases
_				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
	_			antagonists of the invention)	Crohn's disease, multiple
				include assays disclosed in	sclerosis and/or as described
	-			Berger et al., Gene 66:1-10	below), immunodeficiencies
				(1998); Cullen and Malm,	(e.g., as described below),
				Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and

suppressing a T cell-mediated			include inflammation and	re inflammatory disorders, and	treating joint damage in		arthritis. An additional highly	are preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	that (e.g., leukemia, lymphoma,	these and/or as described below		Disorders"). Additionally,		include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metanlasia and/or dysnlasia
Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.						•							
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Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").		A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the
		Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or
	CD152 in Human T cells	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1240	1240
	HLDRM43	HLDRM43
	292	292

		routinely modified to assess	invention includes a method
		the ability of nolvnentides of	for inhihiting and othelial cell
		the applied of polypeptides of	
		the invention (including	growth. A highly preferred
		antibodies and agonists or	embodiment of the invention
		antagonists of the invention) to	includes a method for
		promote or inhibit cell	stimulating endothelial cell
		proliferation, activation, and	proliferation. An alternative
		apoptosis. Exemplary assays	highly preferred embodiment
		for JNK and p38 kinase	of the invention includes a
		activity that may be used or	method for inhibiting
		routinely modified to test JNK	endothelial cell proliferation.
		and p38 kinase-induced	A highly preferred
		activity of polypeptides of the	embodiment of the invention
		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating apoptosis of
-		the invention) include the	endothelial cells. An
	•	assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the
		used according to these assays	activation of and/or

			d according to includes a method for	lude human stimulating angiogenisis. An	ells		s which line includes a method for				ascular method for reducing cardiac	-	on.	of the invention includes a	method for inducing cardiac	hypertrophy. Highly	preferred indications include	neoplastic diseases (e.g., as	described below under	"Hyperproliferative	Disorders"), and disorders of	the cardiovascular system	(e.g., heart disease, congestive	heart failure, hypertension,	aortic stenosis,	cardiomyopathy, valvular	regurgitation, left ventricular	dysfunction, atherosclerosis	and atherosclerotic vascular	disease, diabetic nephropathy,
are publicly available (e.g.,	through the ATCC)	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line	venous blood vessels, and are	involved in functions that	include, but are not limited to,	angiogenesis, vascular	permeability, vascular tone,	and immune cell extravasation.										-							
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intracardiac shunt, cardiac	hypertrophy, myocardial	infarction, chronic	hemodynamic overload, and/or	as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and
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cavernous), glomus tumors, telangiectasia, bacillary angiomatosis, hemanzioendothelioma.	angiosarcoma, haemangiopericytoma, lymphangioma, lymphangiosarcoma. Highly preferred indications also	include cancers such as, prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver, and urinary cancer. Preferred indications include benign	pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Highly preferred indications also include arterial disease, such as, atherosclerosis,	hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s disease and Reynaud"s phenomenom, aneurysms, restenosis; venous and lymphatic disorders such as thrombophlebitis, lymphangitis, and

lymphedema; and other
vascular disorders such as
peripheral vascular disease,
and cancer. Highly
preferred indications also
include trauma such as
wounds, burns, and injured
tissue (e.g., vascular injury
such as, injury resulting from
balloon angioplasty, and
atheroschlerotic lesions),
implant fixation, scarring,
ischemia reperfusion injury,
rheumatoid arthritis,
cerebrovascular disease, renal
diseases such as acute renal
failure, and osteoporosis.
Additional highly preferred
indications include stroke,
graft rejection, diabetic or
other retinopathies, thrombotic
and coagulative disorders,
vascularitis, lymph
angiogenesis, sexual disorders,
age-related macular
degeneration, and treatment
/prevention of endometriosis
and related conditions.
Additional highly preferred
indications include fibromas,
heart disease, cardiac arrest,

					heart valve disease, and
					vascular disease
					Preferred indications include
					blood disorders (e.g., as
			-		described below under
					"Immune Activity", "Blood-
-					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
~_~					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
	HLDRM43	1240	Production of	RANTES FMAT. Assays for	
292			RANTES in	immunomodulatory proteins	
			endothelial cells	that induce chemotaxis of T	
			(such as human	cells, monocytes, and	
			umbilical vein	eosinophils are well known in	
			endothelial cells	the art and may be used or	
			(HUVEC))	routinely modified to assess	

the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as RANTES, and the induction of chemotactic responses in immune cells. Such assays that may be used or routinely modified to test invention	(including antibodies and agonists or antagonists of the invention) include the assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204 (1999); Rowland et al., "Lymphocytes: a practical approach" Chapter 6:138-160 (2000): Cocchi et al., Science 270(5243):1811-1815 (1995); and Robinson et al., Clin Exp Immunol 101(3):398-407

	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described
which are herein incorporated by reference in its entirety. Endothelial cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary endothelial cells that may be used according to these assays include human umbilical vein endothelial cells (HUVEC), which are endothelial cells which line venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate serum response factors and modulate the
	Activation of transcription through serum response element in immune cells (such as natural killer cells).
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		_												_														_		
below under "Immune	Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn"s disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and
expression of genes involved	in growth and upregulate the	function of growth-related	genes in many cell types.	Exemplary assays for	transcription through the SRE	that may be used or routinely	modified to test SRE activity	of the polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Benson	et al., J Immunol 153(9):3862-	3873 (1994); and Black et al.,	Virus Genes 12(2):105-117	(1997), the content of each of	which are herein incorporated	by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary T cells that may be	used according to these assays	include the NK-YT cell line,
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	which is a human natural killer	cancers, such as, for example,
	cell line with cytolytic and	leukemia, lymphoma.
	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other
		preferred indications include
		benign dysproliferative
		disorders and pre-neoplastic
-		conditions, such as, for
		example, hyperplasia,
		metaplasia, and/or dysplasia.
		Preferred indications include
		anemia, pancytopenia,
		leukopenia, thrombocytopenia,
 		Hodgkin's disease, acute
		lymphocytic anemia (ALL),
 		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
 		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune
 		reactions to transplanted
		organs and tissues, hemophilia,
 		hypercoagulation, diabetes
		mellitus, endocarditis,
		meningitis, Lyme Disease,

				cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
 HLDRM43	1240	Activation of transcription through CD28 response element in immune cells (such	Assays for the activation of transcription through the CD28 response element are well-known in the art and may be used or routinely modified to	A highly preferred embodiment of the invention includes a method for stimulating T cell proliferation. An alternative highly preferred
		as T-cells).	assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate IL-2 expression in T cells.	embodiment of the invention includes a method for inhibiting T cell proliferation. A highly preferred embodiment of the invention includes a method for
			Exemplary assays for transcription through the CD28 response element that may be used or routinely modified to test CD28-response element activity of polypeptides of the invention (including antibodies and agonists or antagonists of	activating T cells. An alternative highly preferred embodiment of the invention includes a method for inhibiting the activation of and/or inactivating T cells. A highly preferred embodiment of the invention
			the invention) include assays disclosed in Berger et al., Gene 66:1-10 (1998); Cullen and Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA	includes a method for stimulating (e.g., increasing) IL-2 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g.,

reducing) IL-2 production. Additional highly preferred indications include inflammation and	Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiencies (e.g., as immunodeficiencies (e.g., as	described below), boosting a T cell-mediated immune response, and suppressing a T cell-mediated immune response. Highly preferred indications include neoplastic diseases (e.g., melanoma, renal cell carcinoma, leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Highly preferred indications include neoplasms and cancers, such as, for example, melanoma (e.g.,	metastatic melanoma), renal cell carcinoma (e.g., metastatic renal cell carcinoma), leukemia, lymphoma (e.g., T
85:6342-6346 (1988); McGuire and Iacobelli, J Immunol 159(3):1319-1327 (1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and Butscher et al., J Biol Chem 3(1):552-560 (1998), the contents of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	according to these assays are publicly available (e.g., through the ATCC). Exemplary human T cells that may be used according to these assays include the SUPT cell line, which is a suspension culture of IL-2 and IL-4 responsive T cells.	

rostate,	breast, lung, colon, pancreatic,	brain,	liver and urinary cancer. Other	nclude	Ð	olastic	¥		plasia.	ication	2.3	AIDS, tuberculosis, infections	associated with granulomatous	sis,	low	ase"). A	ation is	ghly	nclude	e	eq	uveitis,	spastic	red	poc	ribed	•	ated	
cell lymphoma), and prostate,	olon, pa	esophageal, stomach, brain,	ry cance	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	A highly preferred indication	includes infection (e.g.,	losis, in	n granul	disease, and osteoporosis,	and/or as described below	under "Infectious Disease")	highly preferred indication is	AIDS. Additional highly	preferred indications include	suppression of immune	reactions to transplanted	organs and/or tissues, uveitis,	psoriasis, and tropical spastic	Preferred	indications include blood	disorders (e.g., as described	below under "Immune	Activity", "Blood-Related	d/or
nphome	lung, co	igeal, sto	nd urina	ed indic	dyspro	ers and 1	ons, suc	le, hype	asia, an	ly prefe	es infect	tubercu	ted witl	e, and os	as desci	'Infection	preferre	Addit	ed indic	ssion of	ns to tra	and/or	is, and		ions inc	ers (e.g.	under "	y", "Blo	arc" on
cell lyr	breast,	esopha	liver a	preferr	benign	disorde	conditi	examp	metapl	A high	include	AIDS,	associa	disease	and/or	, nuder	highly	AIDS.	preferr	suppre	reactio	organs	psorias	paraparesis.	indicat	disorde	below	Activit	D:00.0
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Preferred indications also include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.	A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"),
	Assays for the activation of transcription through the Serum Response Element (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate the serum response factors and modulate the expression of genes involved in growth. Exemplary assays for transcription through the SRE that may be used or
	Activation of transcription through serum response element in immune cells (such as T-cells).
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	293

	routinely modified to test SRE	Highly preferred indications
 	activity of the polypeptides of	include autoimmune diseases
	the invention (including	(e.g., rheumatoid arthritis,
	antibodies and agonists or	systemic lupus erythematosis,
 	antagonists of the invention)	Crohn"s disease, multiple
	include assays disclosed in	sclerosis and/or as described
	Berger et al., Gene 66:1-10	below), immunodeficiencies
	(1998); Cullen and Malm,	(e.g., as described below),
 	Methods in Enzymol 216:362-	boosting a T cell-mediated
	368 (1992); Henthorn et al.,	immune response, and
	Proc Natl Acad Sci USA	suppressing a T cell-mediated
	85:6342-6346 (1988); and	immune response. Additional
	Black et al., Virus Genes	highly preferred indications
	12(2):105-117 (1997), the	include inflammation and
	content of each of which are	inflammatory disorders, and
	herein incorporated by	treating joint damage in
	reference in its entirety. T	patients with rheumatoid
	cells that may be used	arthritis. An additional highly
	according to these assays are	preferred indication is sepsis.
	publicly available (e.g.,	Highly preferred indications
	through the ATCC).	include neoplastic diseases
	Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
	may be used according to these	and/or as described below
	assays include the CTLL cell	under "Hyperproliferative
	line, which is an IL-2	Disorders"). Additionally,
	dependent suspension culture	highly preferred indications
	of T cells with cytotoxic	include neoplasms and
	activity.	cancers, such as, for example,
 		leukemia, lymphoma,
		melanoma, glioma (e.g.,
		malignant glioma), solid

tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	cardiac reperfusion injury, and	asthma and allergy. An	additional preferred indication	is infection (e.g., an infectious
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	-			-																										

					disease as described below under "Infectious Disease").
	HLHFP03	1242	Activation of T-	Kinase assay. JNK and p38	Preferred indications include
294			Cell p38 or JNK	kinase assays for signal	neoplastic diseases (e.g., as
			Signaling Pathway.	transduction that regulate cell	described below under
				proliferation, activation, or	"Hyperproliferative
				apoptosis are well known in	Disorders"), blood disorders
				the art and may be used or	(e.g., as described below under
				routinely modified to assess	"Immune Activity",
				the ability of polypeptides of	"Cardiovascular Disorders",
				the invention (including	and/or "Blood-Related
				antibodies and agonists or	Disorders"), and infection
				antagonists of the invention) to	(e.g., an infectious disease as
				promote or inhibit immune cell	described below under
				(e.g. T-cell) proliferation,	"Infectious Disease"). Highly
				activation, and apoptosis.	preferred indications include
-				Exemplary assays for JNK and	autoimmune diseases (e.g.,
				p38 kinase activity that may be	rheumatoid arthritis, systemic
				used or routinely modified to	lupus erythematosis, multiple
				test JNK and p38 kinase-	sclerosis and/or as described
				induced activity of	below) and
				polypeptides of the invention	immunodeficiencies (e.g., as
				(including antibodies and	described below). Additional
				agonists or antagonists of the	highly preferred indications
				invention) include the assays	include inflammation and
				disclosed in Forrer et al., Biol	inflammatory disorders.
			-	Chem 379(8-9):1101-1110	Highly preferred indications
	-			(1998); Gupta et al., Exp Cell	also include neoplastic
				Res 247(2): 495-504 (1999);	diseases (e.g., leukemia,
				Kyriakis JM, Biochem Soc	lymphoma, and/or as described
				Symp 64:29-48 (1999); Chang	below under

				and Karin, Nature 410(6824):37-40 (2001); and	"Hyperproliferative Disorders"), Highly preferred
				Cobb MH, Prog Biophys Mol	indications include neoplasms
				Biol 71(3-4):479-500 (1999);	and cancers, such as, leukemia,
				the contents of each of which	lymphoma, prostate, breast,
				are herein incorporated by	lung, colon, pancreatic,
				reference in its entirety. T	esophageal, stomach, brain,
				cells that may be used	liver, and urinary cancer. Other
·				according to these assays are	preferred indications include
				publicly available (e.g.,	benign dysproliferative
				through the ATCC).	disorders and pre-neoplastic
				Exemplary mouse T cells that	conditions, such as, for
				may be used according to these	example, hyperplasia,
				assays include the CTLL cell	metaplasia, and/or dysplasia.
				line, which is an IL-2	Preferred indications include
				dependent suspension-culture	arthritis, asthma, AIDS,
				cell line with cytotoxic	allergy, anemia, pancytopenia,
				activity.	leukopenia, thrombocytopenia,
					Hodgkin"s disease, acute
		~			lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
		-			granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
294	HLHFP03	1242	SEAP in HIB/CRE		
	HLHFP03	1242	VEGF in HT1080		

294					
	HLHFP03	1242	Production of	Assays for measuring	Highly preferred indications
294			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
-				agonists or antagonists of the	inflammatory disorders,
- - -				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
				functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
-				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
				endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other
				commercial sources. The	preferred indications include
				expression of VCAM	benign dysproliferative
				(CD106), a membrane-	disorders and pre-neoplastic
				associated protein, can be	conditions, such as, for

	HI UEDO3	C. C	SEAD in OF 21	upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	example, hyperplasia, metaplasia, and/or dysplasia.
294	HLHFFU3	747	SEAF in OE-21		
295	HLHFR58	1243	Production of TNF alpha by dendritic cells	TNFa FMAT. Assays for immunomodulatory proteins produced by activated macrophages, T cells, fibroblasts, smooth muscle, and other cell types that exert a wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins	A highly preferred embodiment of the invention includes a method for inhibiting (e.g., decreasing) TNF alpha production. An alternative highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha production. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lunus erythematosis.

				assays may be isolated using	benign dysproliferative
				techniques disclosed herein or	disorders and pre-neoplastic
				otherwise known in the art.	conditions, such as, for
				Human dendritic cells are	example, hyperplasia,
-×				antigen presenting cells in	metaplasia, and/or dysplasia.
				suspension culture, which,	Preferred indications include
				when activated by antigen	anemia, pancytopenia,
				and/or cytokines, initiate and	leukopenia, thrombocytopenia,
				upregulate T cell proliferation	Hodgkin's disease, acute
				and functional activities.	lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
 -					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
-					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
295	HLHFR58	1243	RANTES in Human T cells		
	HLIBD68	1244	Production of IL-6	IL-6 FMAT. IL-6 is produced	A highly preferred

by T cells and has strong effects on B cells. IL-6 participates in IL-4 induclgE production and increal gA production (IgA play role in mucosal immunity IL-6 induces cytotoxic T Deregulated expression o has been linked to autoim disease, plasmacytomas, myelomas, and chronic hyperproliferative disease Assays for immunomodul and differentiation factor proteins produced by a language of cells where the expression level is strong regulated by cytokines, gradiated by cytokines, gradiate	by T cells and has strong embodiment of the invention	cells. IL-6 includes a method for	participates in IL-4 induced stimulating (e.g., increasing)	IgE production and increases IL-6 production. An alternative	IgA production (IgA plays a highly preferred embodiment		IL-6 induces cytotoxic T cells. method for inhibiting (e.g.,				and chronic of mucosal immunity. Highly	hyperproliferative diseases. preferred indications include	Assays for immunomodulatory blood disorders (e.g., as	and differentiation factor described below under	proteins produced by a large "Immune Activity", "Blood-	variety of cells where the Related Disorders", and/or	expression level is strongly ("Cardiovascular Disorders"),	regulated by cytokines, growth and infection (e.g., as	factors, and hormones are well described below under	known in the art and may be "Infectious Disease"). Highly	used or routinely modified to preferred indications include	ility of autoimmune diseases (e.g.,	polypeptides of the invention rheumatoid arthritis, systemic	ntibodies and lupus erythematosis, multiple	agonists or antagonists of the sclerosis and/or as described		lulation and immunodeficiencies (e.g., as	differentiation and modulate T described below). Highly	cell proliferation and function. preferred indications also	second that tout from the first of the second to a sell
	by T cells an	effects on B cells. IL-6	participates i	IgE producti	IgA producti	role in muco	IL-6 induces	Deregulated	has been link	disease, plasmacytomas,	myelomas, and chronic	hyperprolifer	Assays for in	and different	proteins prod	variety of cel	expression le	regulated by	factors, and l	known in the	used or routi	assess the ability of	polypeptides	(including an	agonists or a	invention) to mediate	immunomodulation and	differentiatio	cell prolifera	Evenulary account that test for

		evaluate the production of	and alternatively suppressing a
	,	cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
 		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
 		may be used or routinely	disorders. Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
 		diffferentiation activity of	preferred indications include
 *		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
 		agonists or antagonists of the	leukemia, lymphoma,
 		invention) include assays	melanoma, and/or as described
 		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
 		approach" Chapter 6:138-160	and cancers, such as, myeloma,
 		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
 		Immunol 158:2919-2925	lymphoma, melanoma, and
 		(1997), the contents of each of	prostate, breast, lung, colon,
 		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
 		be used according to these	indications include benign
 		assays may be isolated using	dysproliferative disorders and
 		techniques disclosed herein or	pre-neoplastic conditions, such
 		otherwise known in the art.	as, for example, hyperplasia,
 		Human dendritic cells are	metaplasia, and/or dysplasia.
		antigen presenting cells in	Preferred indications include

		(including antibodies and	infection (e.g., an infectious
		 agonists or antagonists of the	disease as described below
		invention) to mediate	under "Infectious Disease").
		immunomodulation, modulate	Preferred indications include
		chemotaxis, and modulate T	blood disorders (e.g., as
		cell differentiation. Exemplary	described below under
- ,		assays that test for	"Immune Activity", "Blood-
		immunomodulatory proteins	Related Disorders", and/or
		evaluate the production of	"Cardiovascular Disorders").
		chemokines, such as	Highly preferred indications
		macrophage inflammatory	include autoimmune diseases
		protein 1 alpha (MIP-1a), and	(e.g., rheumatoid arthritis,
		the activation of	systemic lupus erythematosis,
		monocytes/macrophages and T	multiple sclerosis and/or as
		cells. Such assays that may be	described below) and
		used or routinely modified to	immunodeficiencies (e.g., as
		test immunomodulatory and	described below). Additional
		chemotaxis activity of	highly preferred indications
		polypeptides of the invention	include inflammation and
		(including antibodies and	inflammatory disorders.
		agonists or antagonists of the	Preferred indications also
		invention) include assays	include anemia, pancytopenia,
		disclosed in Miraglia et al., J	leukopenia, thrombocytopenia,
		Biomolecular Screening 4:193-	Hodgkin's disease, acute
		204(1999); Rowland et al.,	lymphocytic anemia (ALL),
	4	"Lymphocytes: a practical	plasmacytomas, multiple
		approach" Chapter 6:138-160	myeloma, Burkitt's lymphoma,
		(2000); Satthaporn and	arthritis, AIDS, granulomatous
		Eremin, J R Coll Surg Ednb	disease, inflammatory bowel
		45(1):9-19 (2001); Drakes et	disease, sepsis, neutropenia,
;		al., Transp Immunol 8(1):17-	neutrophilia, psoriasis,

				29 (2000); Verhasselt et al., J Immunol 158:2919-2925	suppression of immune reactions to transplanted
				(1997); and Nardelli et al., J	organs and tissues, hemophilia,
				Leukoc Biol 65:822-828	hypercoagulation, diabetes
				(1999), the contents of each of	mellitus, endocarditis,
				which are herein incorporated	meningitis, Lyme Disease,
				by reference in its entirety.	asthma, and allergy.
				Human dendritic cells that may	Preferred indications also
				be used according to these	include neoplastic diseases
				assays may be isolated using	(e.g., leukemia, lymphoma,
				techniques disclosed herein or	and/or as described below
				otherwise known in the art.	under "Hyperproliferative
				Human dendritic cells are	Disorders"). Highly preferred
				antigen presenting cells in	indications include neoplasms
				suspension culture, which,	and cancers, such as, leukemia,
				when activated by antigen	lymphoma, prostate, breast,
				and/or cytokines, initiate and	lung, colon, pancreatic,
	-			upregulate T cell proliferation	esophageal, stomach, brain,
				and functional activities.	liver, and urinary cancer. Other
					preferred indications include
					benign dysproliferative
					disorders and pre-neoplastic
	-				conditions, such as, for
	_				example, hyperplasia,
					metaplasia, and/or dysplasia.
*	HLIBD68	1244	Production of TNF	TNFa FMAT. Assays for	A highly preferred
296			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
	-			macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred

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wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,	wide variety of inflammatory and cytotoxic effects on a variety of cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modiate immunomodulation, modulate inflammation and cytotoxicity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytotoxic such as tumor necrosis factor alpha (TNFa), and the induction or inhibition of an inflammatory or cytotoxic response. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in Miraglia et al., J Biomolecular Screening 4:193-204(1999); Rowland et al.,
	-

	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
	(2000); vernassen et al., Eur J	and/or as described below
	(1108): Dahlen et al T	niuci riypeipionicianive Disorders") Additionally
	Immunol 160(7):3585-3593	highly preferred indications
	(1998); Verhasselt et al., J	include neoplasms and
	Immunol 158:2919-2925	cancers, such as, leukemia,
	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
	(1999), the contents of each of	tumors, and prostate, breast,
•	which are herein incorporated	lung, colon, pancreatic,
	by reference in its entirety.	esophageal, stomach, brain,
	Human dendritic cells that may	liver and urinary cancer. Other
	be used according to these	preferred indications include
	assays may be isolated using	benign dysproliferative
	techniques disclosed herein or	disorders and pre-neoplastic
	otherwise known in the art.	conditions, such as, for
	Human dendritic cells are	example, hyperplasia,
	antigen presenting cells in	metaplasia, and/or dysplasia.
	suspension culture, which,	Preferred indications include
	when activated by antigen	anemia, pancytopenia,
	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
	upregulate T cell proliferation	Hodgkin's disease, acute
	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,
		neutrophilia, psoriasis,
		suppression of immune

					reactions to transplanted
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLIBD68	1244	Stimulation of	Assays for measuring secretion	A highly preferred
296			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
		-		is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
			-,	also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental

	used or routinely modified to	confusion, drowsiness,
	test for stimulation of insulin	nonketotic hyperglycemic-
	secretion (from pancreatic	hyperosmolar coma,
	cells) by polypeptides of the	cardiovascular disease (e.g.,
	invention (including antibodies	heart disease, atherosclerosis,
	and agonists or antagonists of	microvascular disease,
	the invention) include assays	hypertension, stroke, and other
	disclosed in: Ahren, B., et al.,	diseases and disorders as
	Am J Physiol, 277(4 Pt	described in the
	2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
 	al., Endocrinology,	section below), dyslipidemia,
	138(9):3735-40 (1997); Kim,	endocrine disorders (as
	K.H., et al., FEBS Lett,	described in the "Endocrine
	377(2):237-9 (1995); and,	Disorders" section below),
 	Miraglia S et. al., Journal of	neuropathy, vision impairment
	Biomolecular Screening,	(e.g., diabetic retinopathy and
	4:193-204 (1999), the contents	blindness), ulcers and impaired
	of each of which is herein	wound healing, and infection
	incorporated by reference in its	(e.g., infectious diseases and
-	entirety. Pancreatic cells that	disorders as described in the
	may be used according to these	"Infectious Diseases" section
	assays are publicly available	below, especially of the
 	(e.g., through the ATCC)	urinary tract and skin), carpal
	and/or may be routinely	tunnel syndrome and
 	generated. Exemplary	Dupuytren's contracture).
	pancreatic cells that may be	An additional highly preferred
	used according to these assays	indication is obesity and/or
	include rat INS-1 cells. INS-1	complications associated with
	cells are a semi-adherent cell	obesity. Additional highly
	line established from cells	preferred indications include
	isolated from an X-ray induced weight loss or alternatively,	weight loss or alternatively,

				rat transplantable insulinoma. These cells retain characteristics typical of native pancreatic beta cells including glucose inducible insulin	weight gain. Aditional highly preferred indications are complications associated with insulin resistance.
				secretion. References: Asfari et al. Endocrinology 1992 130:167.	
F0C	HLICQ90	1245	Activation of	Assays for the activation of	A preferred embodiment of
167			transcription through serum	transcription through the Serum Response Element	the invention includes a method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
				antagonists of the invention)	Crohn"s disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies

(e.g., as described below), boosting a T cell-mediated	suppressing a T cell-mediated immune response. Additional	highly preferred indications include inflammation and	inflammatory disorders, and	treating joint damage in patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic
(1998); Cullen and Malm, Methods in Enzymol 216:362-	Proc Natl Acad Sci USA 85:6342-6346 (1988); and	Black et al., Virus Genes 12(2):105-117 (1997), the	content of each of which are	herein incorporated by reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.										
																									

					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
		***************************************			lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
		M			disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
	_	`			reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
	-				is infection (e.g., an infectious
				J	disease as described below
					under "Infectious Disease").
-	HLICQ90	1245	Production of TNF	TNFa FMAT. Assays for	A highly preferred
297		~	alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An

"Lymphocytes: a practical approach" Chapter 6:138-160 (2000); Verhasselt et al., Eur J Immunol 28(11):3886-3890 (1198); Dahlen et al., J Immunol 160(7):3585-3593 (1998); Verhasselt et al., J Immunol 158:2919-2925 (1997); and Nardelli et al., J Leukoc Biol 65:822-828 (1999), the contents of each of which are herein incorporated by reference in its entirety.	include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, leukemia, lymphoma, melanoma, glioma (e.g., malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain,
Human dendritic cells that may be used according to these assays may be isolated using techniques disclosed herein or otherwise known in the art. Human dendritic cells are antigen presenting cells in suspension culture, which, when activated by antigen and/or cytokines, initiate and upregulate T cell proliferation and functional activities.	liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel neutrophilia, psoriasis,

suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").	art indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel ling to blockage, heart disease, stroke, impotence (e.g., due to diabetic neuropathy or blood vessel
	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mobilize calcium. For example, the FLPR assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much higher extracellular calcium. Extracellular factors can cause an influx of calcium, leading to activation of calcium responsive signaling pathways
	Stimulation of Calcium Flux in pancreatic beta cells.
	1245
	HLICQ90
	297

		and alterations in cell	blockage), seizures, mental
	-	functions. Exemplary assays	confusion, drowsiness,
		that may be used or routinely	nonketotic hyperglycemic-
		modified to measure calcium	hyperosmolar coma,
		flux by polypeptides of the	cardiovascular disease (e.g.,
		invention (including antibodies	heart disease, atherosclerosis,
		and agonists or antagonists of	microvascular disease,
		the invention) include assays	hypertension, stroke, and other
		disclosed in: Satin LS, et al.,	diseases and disorders as
		Endocrinology, 136(10):4589-	described in the
		601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
		Endocrinology, 136(7):2960-6	section below), dyslipidemia,
		(1995); Richardson SB, et al.,	endocrine disorders (as
	,	Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
		(1992); and, Meats, JE, et al.,	Disorders" section below),
		Cell Calcium 1989 Nov-	neuropathy, vision impairment
		Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
		contents of each of which is	blindness), ulcers and impaired
		herein incorporated by	wound healing, and infection
		reference in its entirety.	(e.g., infectious diseases and
		Pancreatic cells that may be	disorders as described in the
		used according to these assays	"Infectious Diseases" section
		are publicly available (e.g.,	below, especially of the
		through the ATCC) and/or	urinary tract and skin), carpal
		may be routinely generated.	tunnel syndrome and
		Exemplary pancreatic cells that	Dupuytren's contracture).
	_	may be used according to these	An additional highly preferred
		assays include HITT15 Cells.	indication is obesity and/or
		HITT15 are an adherent	complications associated with
	,	epithelial cell line established	obesity. Additional highly
!		from Syrian hamster islet cells	preferred indications include

				transformed with SV40. These	weight loss or alternatively,
				cells express glucagon,	weight gain. Aditional
				somatostatin, and	highly preferred indications are
				glucocorticoid receptors. The	complications associated with
	,			cells secrete insulin, which is	insulin resistance.
				stimulated by glucose and	
				glucagon and suppressed by	
				somatostatin or	
			,	glucocorticoids. ATTC# CRL-	
				1777 Refs: Lord and	
				Ashcroft. Biochem. J. 219:	
				547-551; Santerre et al. Proc.	
				Natl. Acad. Sci. USA 78:	
				4339-4343, 1981.	
	HLICQ90	1245	Stimulation of	Assays for measuring secretion	A highly preferred
297			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
	-			antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
	_			also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,

s. t may be liffed to insulin eatic	g antibodies agonists of de assays, B., et al., 4 Pt	of of tents in its that	available below, especially of the urinary tract and skin), carpal tunnel syndrome and Dupuytren's contracture). I may be An additional highly preferred inese assays indication is obesity and/or
disregulation is a key component in diabetes. Exemplary assays that may be used or routinely modified to test for stimulation of insulin secretion (from pancreatic	invention (including antibodies and agonists or antagonists of the invention) include assays disclosed in: Ahren, B., et al., Am J Physiol, 277(4 Pt 2):R959-66 (1999); Li, M., et	al., Endocrinology, 138(9):3735-40 (1997); Kim, K.H., et al., FEBS Lett, 377(2):237-9 (1995); and, Miraglia S et. al., Journal of Biomolecular Screening, 4:193-204 (1999), the contents of each of which is herein incorporated by reference in its entirety. Pancreatic cells that	may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary pancreatic cells that may be used according to these assays

				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
	-			These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
				et al. Endocrinology 1992	
				130:167.	
	HLMB076	1246	Activation of	Assays for the activation of	A preferred embodiment of
298			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as natural killer	routinely modified to assess	highly preferred embodiment
		-	cells).	the ability of polypeptides of	of the invention includes a
				the invention (including	method for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,

10 .:	of the polypeptides of the	Crohn"s disease, multiple
31	and agonists or antagonists of	below), immunodeficiencies
th	the invention) include assays	(e.g., as described below),
ip	disclosed in Berger et al., Gene	boosting a T cell-mediated
)9	66:1-10 (1998); Cullen and	immune response, and
<u>N</u>	Malm, Methods in Enzymol	suppressing a T cell-mediated
2.	216:362-368 (1992); Henthorn	immune response. Additional
	et al., Proc Natl Acad Sci USA	highly preferred indications
<u>~</u>	85:6342-6346 (1988); Benson	include inflammation and
et	et al., J Immunol 153(9):3862-	inflammatory disorders, and
38	3873 (1994); and Black et al.,	treating joint damage in
Λ	Virus Genes 12(2):105-117	patients with rheumatoid
	(1997), the content of each of	arthritis. An additional highly
M	which are herein incorporated	preferred indication is sepsis.
	by reference in its entirety. T	Highly preferred indications
3	cells that may be used	include neoplastic diseases
36	according to these assays are	(e.g., leukemia, lymphoma,
Id.	publicly available (e.g.,	and/or as described below
tp	through the ATCC).	under "Hyperproliferative
	Exemplary T cells that may be	Disorders"). Additionally,
3n	used according to these assays	highly preferred indications
<u></u>	include the NK-YT cell line,	include neoplasms and
A .	which is a human natural killer	cancers, such as, for example,
33	cell line with cytolytic and	leukemia, lymphoma,
5	cytotoxic activity.	melanoma, glioma (e.g.,
		malignant glioma), solid
		tumors, and prostate, breast,
		lung, colon, pancreatic,
		esophageal, stomach, brain,
		liver and urinary cancer. Other

					f 1: 1: 1: 1: 1. 1.
				-	preferen marcanons merude
		-			benign dysproliferative
					disorders and pre-neoplastic
					conditions, such as, for
					example, hyperplasia,
					metaplasia, and/or dysplasia.
	,				Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
-					plasmacytomas, multiple
	-				myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
1.0					disease, neutropenia,
		-			neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
•					mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
0	HLQBE09	1247	Production of IL-8	Assay that measures the	Highly preferred indications
299			by immune cells	production of the chemokine	include eosinophilia, asthma,

			(cure of the human	interlantin Q (II Q) from	ollowar branchagasitinity
			Such as the inditial	111CIICANIII-8 (1L-8) [10111	aneigy, hyperschaining
			EUL-1 eosinopnii	Immune cells (such as the	reactions, inflammation, and
			(cells)	EOL-1 human eosinophil cell	inflammatory disorders.
				line) are well known in the art	Additional highly preferred
				(for example, measurement of	indications include immune
				IL-8 production by FMAT)	and hematopoietic disorders
				and may be used or routinely	(e.g., as described below under
				modified to assess the ability	"Immune Activity", and
				of polypeptides of the	"Blood-Related Disorders"),
				invention (including antibodies	autoimmune diseases (e.g.,
				and agonists or antagonists of	rheumatoid arthritis, systemic
				the invention) to promote or	lupus erythematosis, Crohn"s
-				inhibit. Eosinophils are a type	disease, multiple sclerosis
				of immune cell important in	and/or as described below),
-				allergic responses; they are	immunodeficiencies (e.g., as
				recruited to tissues and	described below). Highly
				mediate the inflammtory	preferred indications also
				response of late stage allergic	include boosting or inhibiting
				reaction. IL8 is a strong	immune cell proliferation.
				immunomodulator and may	Preferred indications include
				have a potential	neoplastic diseases (e.g.,
				proinflammatory role in	leukemia, lymphoma, and/or as
				immunological diseases and	described below under
				disorders (such as allergy and	"Hyperproliferative
				asthma).	Disorders"). Highly preferred
					indications include boosting an
					eosinophil-mediated immune
					response, and suppressing an
					eosinophil-mediated immune
					response.
	HLQBE09	1247	SEAP in HIB/CRE		

299					
299	НГОВЕ09	1247	CD71 in Human T cells		
299	HLQBE09	1247	IL-10 in Human T-cell 293T		
299	HLQBE09	1247	TNFa in Human T- cell 2B9		
300	HLQDR48	1248	Activation of Adipocyte ERK	Kinase assay. Kinase assays, for example an Elk-1 kinase	A highly preferred embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
		~		modified to assess the ability	method for inhibiting
				of polypeptides of the	adipocyte proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
				the invention) to promote or	method for stimulating
				inhibit cell proliferation,	adipocyte differentiation. An
				activation, and differentiation.	alternative highly preferred
				Exemplary assays for ERK	embodiment of the invention
		**		kinase activity that may be	includes a method for
				used or routinely modified to	cyte
-774	-			test ERK kinase-induced	differentiation. A highly
		·		activity of polypeptides of the	preferred embodiment of the
				invention (including antibodies	invention includes a method
				and agonists or antagonists of	for stimulating (e.g.,
				the invention) include the	increasing) adipocyte
				assays disclosed in Forrer et	activation. An alternative
				al., Biol Chem 379(8-9):1101-	highly preferred embodiment

of the invention includes a method for inhibiting the activation of (e.g., decreasing) and/or inactivating adipocytes.	Highly preferred indications include endocrine disorders (e.g., as described below under "Endocrine Disorders").	Highly preferred indications also include neoplastic diseases (e.g., lipomas, liposarcomas, and/or as	described below under "Hyperproliferative Disorders"). Preferred	indications include blood disorders (e.g., hypertension, congestive heart failure, blood vessel blockage, heart disease, stroke, impotence and/or as	"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders	"Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"), and infection (e.g., as
1110 (1998); Le Marchand- Brustel Y, Exp Clin Endocrinol Diabetes 107(2):126-132 (1999);	Kyriakis JM, Biochem Soc Symp 64:29-48 (1999); Chang and Karin, Nature 410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol Biol 71(3-4):479-500 (1999); the contents of each of which are herein incorporated by	Mouse adipocyte cells that may be used according to these	assays are publicly available (e.g., through the ATCC). Exemplary mouse adipocyte cells that may be used according to these assays	is an adherent mouse preadipocyte cell line that is a continuous substrain of 3T3 fibroblast cells developed through clonal isolation and	undergo a pre-adipocyte to adipose-like conversion under appropriate differentiation conditions known in the art.
,						

		described helow under
		מכפכווסכם סכוס שוותכו
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
-		indication is a complication
		associated with diabetes (e.g.,
		diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
		hyperosmolar coma,
		cardiovascular disease (e.g.,
		heart disease, atherosclerosis,
		microvascular disease,
		hypertension, stroke, and other
		diseases and disorders as
		described in the

		"Cardiovascular Disorders"
		section below), dyslipidemia,
		endocrine disorders (as
		described in the "Endocrine
		Disorders" section below),
,		neuropathy, vision impairment
		(e.g., diabetic retinopathy and
		blindness), ulcers and impaired
		wound healing, infection (e.g.,
		infectious diseases and
	 -	disorders as described in the
		"Infectious Diseases" section
	•	below (particularly of the
		urinary tract and skin). An
		additional highly preferred
		indication is obesity and/or
		complications associated with
	 	obesity. Additional highly
		preferred indications include
		weight loss or alternatively,
		weight gain. Additional
		highly preferred indications are
		complications associated with
	-	insulin resistance.
		Additional highly preferred
		indications are disorders of the
		musculoskeletal systems
		including myopathies,
		muscular dystrophy, and/or as
		described herein.
		Additional highly preferred

_	-				indications include.
-					hypertension, coronary artery
					disease, dyslipidemia,
					gallstones, osteoarthritis,
•			•		degenerative arthritis, eating
	_				disorders, fibrosis, cachexia,
					and kidney diseases or
					disorders. Preferred
					indications include neoplasms
-					and cancer, such as,
					lymphoma, leukemia and
		•			breast, colon, and kidney
_					cancer. Additional preferred
			·		indications include melanoma,
_					prostate, lung, pancreatic,
-					esophageal, stomach, brain,
	_				liver, and urinary cancer.
					Highly preferred indications
			-		include lipomas and
	_				liposarcomas. Other preferred
	_			*	indications include benign
					dysproliferative disorders and
			-		pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
HLQDR48	 &+	1248	Production of	MCP-1 FMAT. Assays for	A highly preferred
300			MCP-1	immunomodulatory proteins	embodiment of the invention
_	,			that are produced by a large	includes a method for
-				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred

cel	cells are well known in the art	embodiment of the invention
and	and may be used or routinely	includes a method for
om	modified to assess the ability	inhibiting (e.g., reducing)
of j	of polypeptides of the	MCP-1 production. A highly
vni	invention (including antibodies	is
and	and agonists or antagonists of	infection (e.g., an infectious
the	the invention) to mediate	disease as described below
mi	immunomodulation, induce	under "Infectious Disease").
che	chemotaxis, and modulate	Additional highly preferred
mi	immune cell activation.	indications include
Exe	Exemplary assays that test for	inflammation and
imi	immunomodulatory proteins	inflammatory disorders.
 eva	evaluate the production of cell	Preferred indications include
sur	surface markers, such as	blood disorders (e.g., as
om	monocyte chemoattractant	described below under
pro	protein (MCP), and the	"Immune Activity", "Blood-
act	activation of monocytes and T	Related Disorders", and/or
cel	cells. Such assays that may be	"Cardiovascular Disorders").
asn	used or routinely modified to	Highly preferred indications
l tes	test immunomodulatory and	include autoimmune diseases
 Jip diff	diffferentiation activity of	(e.g., rheumatoid arthritis,
lod	polypeptides of the invention	systemic lupus erythematosis,
	(including antibodies and	multiple sclerosis and/or as
 agc	agonists or antagonists of the	described below) and
 vai	invention) include assays	immunodeficiencies (e.g., as
 dis	disclosed in Miraglia et al., J	described below). Preferred
Bic	Biomolecular Screening 4:193-	indications also include
 707	204(1999); Rowland et al.,	anemia, pancytopenia,
	"Lymphocytes: a practical	leukopenia, thrombocytopenia,
 da	approach" Chapter 6:138-160	Hodgkin's disease, acute
(20	(2000); Satthaporn and	lymphocytic anemia (ALL),

plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis. AIDS granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia, neutrophilia, psoriasis.	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis (bacterial and	viral), Lyme Disease, asthma,	and allergy Preferred	indications also include	neoplastic diseases (e.g.,	leukemia, lymphoma, and/or as	described below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,
Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and Verhasselt et al. I Immunol	158:2919-2925 (1997), the	contents of each of which are herein incorporated by	reference in its entirety.	Human dendritic cells that may	be used according to these	assays may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human dendritic cells are	antigen presenting cells in	suspension culture, which,	when activated by antigen	and/or cytokines, initiate and	upregulate T cell proliferation	and functional activities.				-								
																							-				-
				-			-																	-			

					metaplasia, and/or dysplasia.
	HLQDR48	1248	Production of TNF	TNFa FMAT. Assays for	A highly preferred
300			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)
				fibroblasts, smooth muscle,	TNF alpha production. An
				and other cell types that exert a	alternative highly preferred
				wide variety of inflammatory	embodiment of the invention
				and cytotoxic effects on a	includes a method for
				variety of cells are well known	stimulating (e.g., increasing)
				in the art and may be used or	TNF alpha production.
				routinely modified to assess	Highly preferred indications
				the ability of polypeptides of	include blood disorders (e.g.,
				the invention (including	as described below under
				antibodies and agonists or	"Immune Activity", "Blood-
				antagonists of the invention) to	Related Disorders", and/or
				mediate immunomodulation,	"Cardiovascular Disorders"),
				modulate inflammation and	Highly preferred indications
				cytotoxicity. Exemplary	include autoimmune diseases
				assays that test for	(e.g., rheumatoid arthritis,
				immunomodulatory proteins	systemic lupus erythematosis,
				evaluate the production of	Crohn"s disease, multiple
				cytokines such as tumor	sclerosis and/or as described
				necrosis factor alpha (TNFa),	below), immunodeficiencies
				and the induction or inhibition	(e.g., as described below),
				of an inflammatory or	boosting a T cell-mediated
				cytotoxic response. Such	immune response, and
				assays that may be used or	suppressing a T cell-mediated
				routinely modified to test	immune response. Additional
				immunomodulatory activity of	highly preferred indications
				polypeptides of the invention	include inflammation and

	O TI	0701			plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
300	HLQDR48	1248	IL-8 in Normal Human Bronchial Epitheliae		
301	HLTAU74	1249	Activation of transcription through AP1 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the AP1 response element are known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to modulate growth and other cell	Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders (e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), and infection

	functions. Exemplary assays	(e.g., an infectious disease as
	for transcription through the	described below under
	AP1 response element that	"Infectious Disease"). Highly
	may be used or routinely	preferred indications include
	modified to test AP1-response	autoimmune diseases (e.g.,
	element activity of	rheumatoid arthritis, systemic
	polypeptides of the invention	lupus erythematosis, multiple
	(including antibodies and	sclerosis and/or as described
	agonists or antagonists of the	below) and
	invention) include assays	immunodeficiencies (e.g., as
	disclosed in Berger et al., Gene	described below). Additional
	66:1-10 (1988); Cullen and	highly preferred indications
	Malm, Methods in Enzymol	include inflammation and
	216:362-368 (1992); Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	reference in its entirety. T	lung, colon, pancreatic,
	cells that may be used	esophageal, stomach, brain,
	according to these assays are	liver, and urinary cancer. Other
 	publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	Exemplary mouse T cells that	disorders and pre-neoplastic
	may be used according to these	conditions, such as, for

				assays include the CTLL cell line, which is an IL-2 dependent suspension-culture	example, hyperplasia, metaplasia, and/or dysplasia. Preferred indications include
				activity.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia, Hodokin's disease acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HLTAU74	1249	Activation of	Kinase assay. Kinase assays,	A highly preferred
301	,		Natural Killer Cell	for example an Elk-1 kinase	embodiment of the invention
			ERK Signaling	assay, for ERK signal	includes a method for
			Pathway.	transduction that regulate cell	stimulating natural killer cell
				proliferation or differentiation	proliferation. An alternative
		·		are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a
				modified to assess the ability	method for inhibiting natural
		-		of polypeptides of the	killer cell proliferation. A
				invention (including antibodies	highly preferred embodiment
				and agonists or antagonists of	of the invention includes a
		-		the invention) to promote or	method for stimulating natural
				inhibit cell proliferation,	killer cell differentiation. An
				activation, and differentiation.	alternative highly preferred

Exemplary assays for ERK	embodiment of the invention
 kinase activity that may be	includes a method for
used or routinely modified to	inhibiting natural killer cell
 test ERK kinase-induced	differentiation. Highly
activity of polypeptides of the	preferred indications include
 invention (including antibodies	neoplastic diseases (e.g., as
 and agonists or antagonists of	described below under
the invention) include the	"Hyperproliferative
assays disclosed in Forrer et	Disorders"), blood disorders
al., Biol Chem 379(8-9):1101-	(e.g., as described below under
 1110 (1998); Kyriakis JM,	"Immune Activity",
Biochem Soc Symp 64:29-48	"Cardiovascular Disorders",
(1999); Chang and Karin,	and/or "Blood-Related
Nature 410(6824):37-40	Disorders"), immune disorders
(2001); and Cobb MH, Prog	(e.g., as described below under
Biophys Mol Biol 71(3-4):479-	
 500 (1999); the contents of	infections (e.g., as described
each of which are herein	below under "Infectious
incorporated by reference in its	Disease"). Preferred
 entirety. Natural killer cells	indications include blood
that may be used according to	disorders (e.g., as described
these assays are publicly	below under "Immune
available (e.g., through the	Activity", "Blood-Related
ATCC). Exemplary natural	Disorders", and/or
killer cells that may be used	"Cardiovascular Disorders").
according to these assays	Highly preferred indications
include the human natural	include autoimmune diseases
killer cell lines (for example,	(e.g., rheumatoid arthritis,
NK-YT cells which have	systemic lupus erythematosis,
cytolytic and cytotoxic	multiple sclerosis and/or as
activity) or primary NK cells.	described below) and

and a construction of the	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include cancers such as,	kidney, melanoma, prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver, urinary cancer,	lymphoma and leukemias.	Other preferred indications	include benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Other highly preferred	indications include,	pancytopenia, leukopenia,	leukemias, Hodgkin's disease,	acute lymphocytic anemia	(ALL), arthritis, asthma,	AIDS, granulomatous disease,	inflammatory bowel disease,	sepsis, psoriasis, immune	reactions to transplanted	organs and tissues,	endocarditis, meningitis, Lyme	
	-					_																								
	-																													_

	HLTDV50	1250	IL-10 in Human T-		
302			cell 2B9		
	HLTDV50	1250	Production of	Assays for measuring	Preferred embodiments of the
302			ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
			•	invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
			_	al., Am J Pathol, 156(5):1733-	
	,			1739 (2000), the contents of	
				each of which is herein	
				incorporated by reference in its	
				entirety. Cells that may be	
·				used according to these assays	
				are publicly available (e.g.,	•
				through the ATCC) and/or	
				may be routinely generated.	
				Exemplary cells that may be	
				used according to these assays	
				include microvascular	
				endothelial cells (MVEC).	

	HLTE125	1251	Activation of	This reporter assay measures	Highly preferred indications
303			transcription	activation of the GATA-3	include allergy, asthma, and
			through GATA-3	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of GATA-3 in mast	(e.g., an infectious disease as
	-		as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the GATA3 response	Preferred indications also
				element are well-known in the	include blood disorders (e.g.,
				art and may be used or	as described below under
				routinely modified to assess	"Immune Activity", "Blood-
				the ability of polypeptides of	Related Disorders", and/or
				the invention (including	"Cardiovascular Disorders").
				antibodies and agonists or	Preferred indications include
				antagonists of the invention) to	autoimmune diseases (e.g.,
				regulate GATA3 transcription	rheumatoid arthritis, systemic
				factors and modulate	lupus erythematosis, multiple
				expression of mast cell genes	sclerosis and/or as described
				important for immune response	below) and
				development. Exemplary	immunodeficiencies (e.g., as
				assays for transcription	described below). Preferred
				through the GATA3 response	indications include neoplastic
				element that may be used or	diseases (e.g., leukemia,
				routinely modified to test	lymphoma, melanoma,
,				GATA3-response element	prostate, breast, lung, colon,
				activity of polypeptides of the	pancreatic, esophageal,
				invention (including antibodies	stomach, brain, liver, and
				and agonists or antagonists of	urinary tract cancers and/or as
				the invention) include assays	described below under

		disclosed in Berger et al., Gene	"Hyperproliferative
		66:1-10 (1998); Cullen and	Disorders"). Other preferred
		Malm, Methods in Enzymol	indications include benign
		216:362-368 (1992); Henthorn	dysproliferative disorders and
		et al., Proc Natl Acad Sci USA	pre-neoplastic conditions, such
		85:6342-6346 (1988); Flavell	as, for example, hyperplasia,
	•	et al., Cold Spring Harb Symp	metaplasia, and/or dysplasia.
-		Quant Biol 64:563-571 (1999);	Preferred indications include
		Rodriguez-Palmero et al., Eur	anemia, pancytopenia,
		J Immunol 29(12):3914-3924	leukopenia, thrombocytopenia,
		(1999); Zheng and Flavell,	leukemias, Hodgkin's disease,
		Cell 89(4):587-596 (1997); and	acute lymphocytic anemia
		Henderson et al., Mol Cell Biol	(ALL), plasmacytomas,
		14(6):4286-4294 (1994), the	multiple myeloma, Burkitt's
		contents of each of which are	lymphoma, arthritis, AIDS,
		herein incorporated by	granulomatous disease,
		reference in its entirety. Mast	inflammatory bowel disease,
		cells that may be used	sepsis, neutropenia,
		according to these assays are	neutrophilia, psoriasis,
		publicly available (e.g.,	suppression of immune
-		through the ATCC).	reactions to transplanted
		Exemplary human mast cells	organs and tissues, hemophilia,
•		that may be used according to	hypercoagulation, diabetes
		these assays include the HMC-	mellitus, endocarditis,
		1 cell line, which is an	meningitis, and Lyme Disease.
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	
		many characteristics of	
		immature mast cells.	

	HLTE125	1251	Activation of	This reporter assay measures	Highly preferred indications
303			transcription	activation of the NFAT	include allergy, asthma, and
			through NFAT	signaling pathway in HMC-1	rhinitis. Additional preferred
			response element in	human mast cell line.	indications include infection
			immune cells (such	Activation of NFAT in mast	(e.g., an infectious disease as
			as mast cells).	cells has been linked to	described below under
				cytokine and chemokine	"Infectious Disease"), and
				production. Assays for the	inflammation and
				activation of transcription	inflammatory disorders.
				through the Nuclear Factor of	Preferred indications also
				Activated T cells (NFAT)	include blood disorders (e.g.,
				response element are well-	as described below under
				known in the art and may be	"Immune Activity", "Blood-
				used or routinely modified to	Related Disorders", and/or
				assess the ability of	"Cardiovascular Disorders").
				polypeptides of the invention	Preferred indications include
				(including antibodies and	autoimmune diseases (e.g.,
				agonists or antagonists of the	rheumatoid arthritis, systemic
				invention) to regulate NFAT	lupus erythematosis, multiple
				transcription factors and	sclerosis and/or as described
		·		modulate expression of genes	below) and
				involved in	immunodeficiencies (e.g., as
				immunomodulatory functions.	described below). Preferred
		-		Exemplary assays for	indications include neoplastic
				transcription through the	diseases (e.g., leukemia,
				NFAT response element that	lymphoma, melanoma,
				may be used or routinely	prostate, breast, lung, colon,
	·			modified to test NFAT-	pancreatic, esophageal,
				response element activity of	stomach, brain, liver, and
				polypeptides of the invention	urinary tract cancers and/or as
				(including antibodies and	described below under

		agonists or antagonists of the	"Hyperproliterative
		invention) include assays	Disorders"). Other preferred
		disclosed in Berger et al., Gene	indications include benign
		66:1-10 (1998); Cullen and	dysproliferative disorders and
		Malm, Methods in Enzymol	pre-neoplastic conditions, such
		216:362-368 (1992); Henthorn	as, for example, hyperplasia,
		et al., Proc Natl Acad Sci USA	metaplasia, and/or dysplasia.
		85:6342-6346 (1988); De Boer	Preferred indications include
		et al., Int J Biochem Cell Biol	anemia, pancytopenia,
		31(10):1221-1236 (1999); Ali	leukopenia, thrombocytopenia,
		et al., J Immunol	leukemias, Hodgkin's disease,
		165(12):7215-7223 (2000);	acute lymphocytic anemia
		Hutchinson and McCloskey, J	(ALL), plasmacytomas,
		Biol Chem 270(27):16333-	multiple myeloma, Burkitt's
		16338 (1995), and Turner et	lymphoma, arthritis, AIDS,
		al., J Exp Med 188:527-537	granulomatous disease,
-		(1998), the contents of each of	inflammatory bowel disease,
		which are herein incorporated	sepsis, neutropenia,
		by reference in its entirety.	neutrophilia, psoriasis,
		Mast cells that may be used	suppression of immune
		according to these assays are	reactions to transplanted
		publicly available (e.g.,	organs and tissues, hemophilia,
		through the ATCC).	hypercoagulation, diabetes
		Exemplary human mast cells	mellitus, endocarditis,
		that may be used according to	meningitis, and Lyme Disease.
		these assays include the HMC-	
		1 cell line, which is an	
		immature human mast cell line	
		established from the peripheral	
		blood of a patient with mast	
		cell leukemia, and exhibits	

				many characteristics of	
				immature mast cells.	
303	HL TEI25	1251	IL-6 in HUVEC		
	HLTEJ06	1252	Activation of	Assays for the activation of	A preferred embodiment of
304	~~~		transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
	_			the invention (including	for stimulating (e.g.,
·				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
				SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,
	,			antagonists of the invention)	Crohn's disease, multiple
				include assays disclosed in	sclerosis and/or as described
				Berger et al., Gene 66:1-10	below), immunodeficiencies
		-		(1998); Cullen and Malm,	(e.g., as described below),
		-		Methods in Enzymol 216:362-	boosting a T cell-mediated
				368 (1992); Henthorn et al.,	immune response, and
ì				Proc Natl Acad Sci USA	suppressing a T cell-mediated

immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,	leukemia, lymphoma,	melanoma, glioma (e.g.,	malignant glioma), solid	tumors, and prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include
85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.														
											-		-		,	,,,														
					_																									

					organia nonotronomia
					alicilla, palicytopellia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLTFA64	1253	Production of	IFNgamma FMAT. IFNg	A highly preferred
305			IFNgamma using	plays a central role in the	embodiment of the invention
			Natural Killer cells	immune system and is	includes a method for
				considered to be a	stimulating the production of
				proinflammatory cytokine.	IFNg. An alternative highly
				IFNg promotes TH1 and	preferred embodiment of the
				inhibits TH2; promotes IgG2a	invention includes a method
				and inhibits IgE; induces	for inhibiting the production of
				macrophage activation; and	IFNg. Highly preferred

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-	d	Assays for immunomodulatory	disorders (e.g., as described
	<u>a</u>	proteins produced by T cells	below under "Immune
	a	and NK cells that regulate a	Activity", "Blood-Related
	>	variety of inflammatory	Disorders",
	g	activities and inhibit TH2	"Hyperproliferative Disorders"
	u	helper cell functions are well	(e.g. cancer/tumorigenesis)
	×	known in the art and may be	and/or "Cardiovascular
	n	used or routinely modified to	Disorders"), and infection
	8	assess the ability of	(e.g., viral infections,
	d	polypeptides of the invention	tuberculosis, infections
		(including antibodies and	associated with chronic
	a	agonists or antagonists of the	granulomatosus disease and
	·i	invention) to mediate	malignant osteoporosis, and/or
	ii	immunomodulation, regulate	as described below under
	<u> </u>	inflammatory activities,	"Infectious Disease"). Highly
	u	modulate TH2 helper cell	preferred indications include
	-	function, and/or mediate	autoimmune disease (e.g.,
	ų	humoral or cell-mediated	rheumatoid arthritis, systemic
	· · · · · · · · · · · · · · · · · · ·	immunity. Exemplary assays	lupus erythematosis, multiple
	T	that test for	sclerosis and/or as described
	<u> </u>	immunomodulatory proteins	below), immunodeficiency
	•	evaluate the production of	(e.g., as described below),
	3	cytokines, such as Interferon	boosting a T cell-mediated
	5.0	gamma (IFNg), and the	immune response, and
	<u>a</u>	activation of T cells. Such	suppressing a T cell-mediated
	<u>a</u>	assays that may be used or	immune response, boosting
	<u> </u>	routinely modified to test	antibody-dependent immune
	· 	immunomodulatory activity of	responses, suppressing
	<u>a</u>	polypeptides of the invention	antibody-dependent immune
		(including antibodies and	responses, boosting innate

		agonists or antagonists of the	immunity and immune
		invention) include the assays	responses, and suppressing
		disclosed in Miraglia et al., J	innate immunity and immune
		Biomolecular Screening 4:193-	responses. Additional highly
		204 (1999); Rowland et al.,	preferred indications include
		"Lymphocytes: a practical	inflammation and
		approach" Chapter 6:138-160	inflammatory disorders.
	-	(2000); Gonzalez et al., J Clin	Additional preferred
,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,		Lab Anal 8(5):225-233 (1995);	indications include idiopathic
		Billiau et al., Ann NY Acad	pulmonary fibrosis. Highly
		Sci 856:22-32 (1998); Boehm	preferred indications include
		et al., Annu Rev Immunol	neoplastic diseases (e.g.,
		15:749-795 (1997), and	leukemia, lymphoma,
		Rheumatology (Oxford)	melanoma, and/or as described
		38(3):214-20 (1999), the	below under
		contents of each of which are	"Hyperproliferative
		herein incorporated by	Disorders"). Highly preferred
		reference in its entirety.	indications include neoplasms
		Natural Killer (NK) cells that	and cancers, such as, for
		may be used according to these	example, leukemia, lymphoma,
		assays are publicly available	melanoma, and prostate,
		(e.g., through the ATCC) or	breast, lung, colon, pancreatic,
		may be isolated using	esophageal, stomach, brain,
		techniques disclosed herein or	liver and urinary cancer. Other
		otherwise known in the art.	preferred indications include
		Natural killer (NK) cells are	benign dysproliferative
		large granular lymphocytes	disorders and pre-neoplastic
	,	that have cytotoxic activity but	conditions, such as, for
:		do bind antigen. NK cells	example, hyperplasia,
	-	show antibody-independent	metaplasia, and/or dysplasia.
		killing of tumor cells and also	Preferred indications include

ut Tuga	23.7	N3C1	15. For For	recognize antibody bound on target cells, via NK Fc receptors, leading to cell-mediated cytotoxicity.	anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
Ĭ	G37	1254	Glucose Production in H4IIE		
HL	Н.Т.Н.С.3.7	1254	Activation of transcription through STAT6 response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Signal Transducers and Activators of Transcription (STAT6) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate STAT6	A highly preferred indication is allergy. Another highly preferred indication is asthma. Additional highly preferred indications include inflammation and inflammatory disorders. Preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-

		transcription factors and	Related Disorders", and/or
		modulate the expression of	"Cardiovascular Disorders").
		multiple genes. Exemplary	Preferred indications include
		assays for transcription	autoimmune diseases (e.g.,
		through the STAT6 response	rheumatoid arthritis, systemic
		element that may be used or	lupus erythematosis, multiple
		routinely modified to test	sclerosis and/or as described
	-	STAT6 response element	below) and
	•	activity of the polypeptides of	immunodeficiencies (e.g., as
		the invention (including	described below).
		antibodies and agonists or	Preferred indications include
		antagonists of the invention)	neoplastic diseases (e.g.,
		include assays disclosed in	leukemia, lymphoma,
		Berger et al., Gene 66:1-10	melanoma, and/or as described
 		(1998); Cullen and Malm,	below under
		Methods in Enzymol 216:362-	"Hyperproliferative
		368 (1992); Henthorn et al.,	Disorders"). Preferred
		Proc Natl Acad Sci USA	indications include neoplasms
		85:6342-6346 (1988); Georas	and cancers, such as, leukemia,
		et al., Blood 92(12):4529-4538	lymphoma, melanoma, and
		(1998); Moffatt et al.,	prostate, breast, lung, colon,
		Transplantation 69(7):1521-	pancreatic, esophageal,
		1523 (2000); Curiel et al., Eur	stomach, brain, liver and
		J Immunol 27(8):1982-1987	urinary cancer. Other preferred
 		(1997); and Masuda et al., J	indications include benign
		Biol Chem 275(38):29331-	dysproliferative disorders and
	,	29337 (2000), the contents of	pre-neoplastic conditions, such
 		each of which are herein	as, for example, hyperplasia,
		incorporated by reference in its	metaplasia, and/or dysplasia.
		entirety. T cells that may be	Preferred indications include
		used according to these assays	anemia, pancytopenia,

				are publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the SUPT cell line,	leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma,
				which is a suspension culture of IL-2 and IL-4 responsive T cells.	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis,
					suppression of immune reactions to transplanted organs and tissues, hemophilia hypercoamlation
					diabetes mellitus, endocarditis, meningitis, and Lyme Disease.
					indication is infection (e.g., an infectious disease as described below under "Infectious
307	HLWAA17	1255	Regulation of transcription of Malic Enzyme in	Assays for the regulation of transcription of Malic Enzyme are well-known in the art and	A highly preferred indication is diabetes mellitus. An additional highly preferred
			adipocytes	may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies	indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephronathy, kidney disease
				and agonists or antagonists of the invention) to regulate	(e.g., renal failure, nephropathy and/or other
				transcription of Malic Enzyme, a key enzyme in lipogenesis.	diseases and disorders as described in the "Renal

Malic enzyme is involved in	Disorders" section below).
lipogenesisand its expression is	diabetic neuropathy, nerve
 stimulted by insulin. ME	disease and nerve damage
 promoter contains two direct	(e.g., due to diabetic
 repeat (DR1)- like elements	neuropathy), blood vessel
 MEp and MEd identified as	blockage, heart disease, stroke,
 putative PPAR response	impotence (e.g., due to diabetic
 elements. ME promoter may	neuropathy or blood vessel
also responds to AP1 and other	blockage), seizures, mental
transcription factors.	confusion, drowsiness,
Exemplary assays that may be	nonketotic hyperglycemic-
used or routinely modified to	hyperosmolar coma,
test for regulation of	cardiovascular disease (e.g.,
transcription of Malic Enzyme	heart disease, atherosclerosis,
 (in adipoocytes) by	microvascular disease,
polypeptides of the invention	hypertension, stroke, and other
(including antibodies and	diseases and disorders as
 agonists or antagonists of the	described in the
 invention) include assays	"Cardiovascular Disorders"
disclosed in: Streeper, R.S., et	section below), dyslipidemia,
 al., Mol Endocrinol,	endocrine disorders (as
 12(11):1778-91 (1998);	described in the "Endocrine
 Garcia-Jimenez, C., et al., Mol	Disorders" section below),
Endocrinol, 8(10):1361-9	neuropathy, vision impairment
(1994); Barroso, I., et al., J	(e.g., diabetic retinopathy and
Biol Chem, 274(25):17997-	blindness), ulcers and impaired
8004 (1999); Ijpenberg, A., et	wound healing, and infection
 al., J Biol Chem,	(e.g., infectious diseases and
272(32):20108-20117 (1997);	disorders as described in the
Berger, et al., Gene 66:1-10	"Infectious Diseases" section
(1988); and, Cullen, B., et al.,	below, especially of the

				Methods in Enzymol.	urinary tract and skin), carpal
				contents of each of which is	Dupuytren's contracture).
				herein incorporated by	An additional highly preferred
				reference in its entirety.	indication is obesity and/or
				Hepatocytes that may be used	complications associated with
				according to these assays are	obesity. Additional highly
				publicly available (e.g.,	preferred indications include
				through the ATCC) and/or	weight loss or alternatively,
				may be routinely generated.	weight gain. Aditional
				Exemplary hepatocytes that	highly preferred indications are
				may be used according to these	complications associated with
				assays includes the H4IIE rat	insulin resistance.
				liver hepatoma cell line.	
	HLWAA17	1255	Production of	Assays for measuring	Preferred embodiments of the
307	1		ICAM-1	expression of ICAM-1 are	invention include using
				well-known in the art and may	polypeptides of the invention
				be used or routinely modified	(or antibodies, agonists, or
				to assess the ability of	antagonists thereof) in
				polypeptides of the invention	detection, diagnosis,
				(including antibodies and	prevention, and/or treatment of
				agonists or antagonists of the	Inflammation, Vascular
				invention) to regulate ICAM-1	Disease, Athereosclerosis,
				expression. Exemplary assays	Restenosis, and Stroke
				that may be used or routinely	
				modified to measure ICAM-1	
				expression include assays	
				disclosed in: Takacs P, et al,	
				FASEB J, 15(2):279-281	
				(2001); and, Miyamoto K, et	
				al., Am J Pathol, 156(5):1733-	

	A highly preferred embodiment of the invention includes a method for stimulating endothelial cell growth. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell growth. A highly preferred embodiment of the invention includes a method for stimulating endothelial cell proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting endothelial cell proliferation. A highly preferred embodiment of the invention embodiment of the invention
each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include microvascular endothelial cells (MVEC).	Kinase assay. JNK and p38 kinase assays for signal transduction that regulate cell proliferation, activation, or apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and apoptosis. Exemplary assays for JNK and p38 kinase activity that may be used or routinely modified to test JNK and p38 kinase-induced activity of polypeptides of the activity of polypeptides of the
	Activation of Endothelial Cell p38 or JNK Signaling Pathway.
	1256
	HLWAA88
	308

		invention (including antibodies	includes a method for
		and agonists or antagonists of	stimulating anontosis of
		alla agollists di allagollists di	summaning apoptosis or
	•	the invention) include the	endothelial cells. An
	-	assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Gupta et al., Exp	includes a method for
		Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
		(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
		Soc Symp 64:29-48 (1999);	A highly preferred
		Chang and Karin, Nature	embodiment of the invention
		410(6824):37-40 (2001); and	includes a method for
		Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
		Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
		the contents of each of which	alternative highly preferred
		are herein incorporated by	embodiment of the invention
		reference in its entirety.	includes a method for
		Endothelial cells that may be	inhibiting (e.g., decreasing) the
		used according to these assays	activation of and/or
		are publicly available (e.g.,	inactivating endothelial cells.
7-7-7		through the ATCC).	A highly preferred
		Exemplary endothelial cells	embodiment of the invention
		that may be used according to	includes a method for
		these assays include human	stimulating angiogenisis. An
		umbilical vein endothelial cells	alternative highly preferred
		(HUVEC), which are	embodiment of the invention
		endothelial cells which line	includes a method for
		venous blood vessels, and are	inhibiting angiogenesis. A
		involved in functions that	highly preferred embodiment
		include, but are not limited to,	of the invention includes a
		angiogenesis, vascular	method for reducing cardiac
		permeability, vascular tone,	hypertrophy. An alternative

highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly preferred indications include neoplastic diseases (e.g., as described below under	"Hyperproliferative Disorders"), and disorders of the cardiovascular system (e.g., heart disease, congestive heart failure, hypertension, aortic stenosis,	cardiomyopathy, valvular regurgitation, left ventricular dysfunction, atherosclerosis and atherosclerotic vascular disease, diabetic nephropathy, intracardiac shunt, cardiac hypertrophy, myocardial infarction, chronic	hemodynamic overload, and/or as described below under "Cardiovascular Disorders"). Highly preferred indications include cardiovascular, endothelial and/or angiogenic disorders (e.g., systemic disorders that affect vessels such as diabetes mellitus, as well as diseases of the vessels
and immune cell extravasation.			

themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi"s sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,	angiosarcoma,	haemangiopericytoma,	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and
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												-																		

dysproliterative disorders and pre-neophastic conditions, such as, for example, hyperplasia, meraplasia, and/or dysplasia, meraplasia, and/or dysplasia, meraplasia, and/or dysplasia, meraplasia, and/or dysplasia, highly preferred indications also include arterial disease, such as, atterosclerosis, hypertension, coronary atery disease, inflammatory vasculitides, Reynard's disease and Reynard's disease and Reynard's phenomenom, aneurysms, restenosis; venous and lymphatocitosis such as thrombophlebitis, lymphatocitosis such as peripheral vascular disorders such as peripheral vascular disease, and examer. Highly preferred indications also include trauma such as and cancer. Highly preferred indications also include trauma such as injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarning, inplant fixation, scarning, inplant fixation, scarning, inplant fixation, scarning, implant fixation, scarning, inplant fixation, scarning, injury injury, include injury, schemia repertision injury, include the scarning, injury injury, siehemia repertision injury, include the scarning injury, implant fixation, injury, i			urinary cancer. Preferred
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as, for example, hyperplasis, metaplasis, and or dysplasis, metaplasis, and or dysplasis, metaplasis, and or dysplasis. Highly preferred inderations also include anterial disease, such as, atterosolerosis, hypertension, coronary artery disease, inflammatory vascultides, Reynaud's disease, inflammatory vascultides, Reynaud's phenomenom, aneurysms, restenosis; venous and hymphatic disorders such as thromopophabeltis, hymphatic disorders such as peripheral vascular disorders such as peripheral vascular disorders such as peripheral vascular disease, and cancer. Highly preferred indications also include frauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschleroite besions), implant fixation, scarring, include raperfusion injury, includent are perfusion, scarring, includent areperfusion injury, includent are perfusion search in include case.	 		dysproliferative disorders and
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Highly preferred indications also include arterial disease, such as, atheroselerosis, hypertension, coronary artery disease, inflammatory vasculitides, Reynaud"s phenomenom, aneurysms, restencois, venous and lymphatic disorders such as thrombophlebitis, lymphagitis, and lymphedema; and other vascular disease, and cancer. Highly preferred indications also include trauma such as wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, isohemia reperfusion rijury,	 		as, for example, hyperplasia,
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wounds, burns, and injured tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,			include trauma such as
tissue (e.g., vascular injury such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	-		wounds, burns, and injured
such as, injury resulting from balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,	 		tissue (e.g., vascular injury
balloon angioplasty, and atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,			such as, injury resulting from
atheroschlerotic lesions), implant fixation, scarring, ischemia reperfusion injury,			balloon angioplasty, and
implant fixation, scarring, ischemia reperfusion injury,			atheroschlerotic lesions),
ischemia reperfusion injury,			implant fixation, scarring,
			ischemia reperfusion injury,

rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as	described below under	("Immune Activity", "Blood-	Related Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described
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	HLWAA88	1256	Production of	RANTES FMAT. Assays for	below) and immunodeficiencies (e.g., as described below). Additional preferred indications include inflammation and inflammatory disorders (such as acute and chronic inflammatory diseases, e.g., inflammatory bowel disease and Crohn's disease), and pain management.
308			RANTES in endothelial cells (such as human umbilical vein endothelial cells (HUVEC))	immunomodulatory proteins that induce chemotaxis of T cells, monocytes, and eosinophils are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate immunomodulation, induce chemotaxis, and/or mediate humoral or cellmediate humoral or cellmediate the production of evaluate the production of cytokines, such as RANTES, and the induction of	

chemotactic responses in	immune cells. Such assays	that may be used or routinely	modified to test	immunomodulatory activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include the assays	disclosed in Miraglia et al., J	Biomolecular Screening 4:193-	204 (1999); Rowland et al.,	"Lymphocytes: a practical	approach" Chapter 6:138-160	(2000): Cocchi et al., Science	270(5243):1811-1815 (1995);	and Robinson et al., Clin Exp	Immunol 101(3):398-407	(1995), the contents of each of	which are herein incorporated	by reference in its entirety.	Endothelial cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary endothelial cells	that may be used according to	these assays include human	umbilical vein endothelial cells	(HUVEC), which are	endothelial cells which line
																				-										

venous blood vessels, and are involved in functions that include, but are not limited to, angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.	Assays for the regulation (i.e. increases or decreases) of viability and proliferation of cells in vitro are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate viability and proliferation of pre-adipose cells and cell lines. For example, the CellTiter-Gloô Luminescent Cell Viability Assay (Promega Corp., Madison, WI, USA) can be used to measure the number of viable cells in culture based on quantitation of the ATP presence of metabolically active cells. 3T3-L1 is a mouse preadipocyte cell line. It is a continuous substrain of
	Proliferation of preadipose cells (such as 3T3-L1 cells)
	1257
	HLWAD77
	309

	tion of A preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) TNF alpha production. An alternative preferred embodiment of the invention includes a method for stimulating (e.g., increasing) TNF alpha sts or increasing) TNF alpha production. Preferred indications include blood disorders (e.g., as described
disclosed in: Richards JD, et al., J Immunol, 166(6):3855-3864 (2001); Dinkel, A, et al., J Exp Med, 188(12):2215-2224 (1998); and, Newton, JS, et al., Eur J Immunol 1996 Apr;26(4):811-816 (1996), the contents of each of which are herein incorporated by reference in its entirety. Immune cells that may be used according to these assays are publicly available (e.g., through the ATCC). Exemplary epithelial cells that may be used assays include the Raji cell line.	Activation of transcription through the through serum Serum Response Element response element in (SRE) are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of factors and modulate the factors and modulate the
	1258 Activation of transcription through serum response eleme immune cells (as T-cells).
	HLWAE11

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Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders"),	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	Crohn's disease, multiple	sclerosis and/or as described	below), immunodeficiencies	(e.g., as described below),	boosting a T cell-mediated	immune response, and	suppressing a T cell-mediated	immune response. Additional	highly preferred indications	include inflammation and	inflammatory disorders, and	treating joint damage in	patients with rheumatoid	arthritis. An additional highly	preferred indication is sepsis.	Highly preferred indications	include neoplastic diseases	(e.g., leukemia, lymphoma,	and/or as described below	under "Hyperproliferative	Disorders"). Additionally,	highly preferred indications	include neoplasms and	cancers, such as, for example,
in growth. Exemplary assays	for transcription through the	SRE that may be used or	routinely modified to test SRE	activity of the polypeptides of	the invention (including	antibodies and agonists or	antagonists of the invention)	include assays disclosed in	Berger et al., Gene 66:1-10	(1998); Cullen and Malm,	Methods in Enzymol 216:362-	368 (1992); Henthorn et al.,	Proc Natl Acad Sci USA	85:6342-6346 (1988); and	Black et al., Virus Genes	12(2):105-117 (1997), the	content of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary mouse T cells that	may be used according to these	assays include the CTLL cell	line, which is an IL-2	dependent suspension culture	of T cells with cytotoxic	activity.
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				leukemia, lymphoma,
 •				melanoma, glioma (e.g.,
 				malignant glioma), solid
_				tumors, and prostate, breast,
 				lung, colon, pancreatic,
 				esophageal, stomach, brain,
				liver and urinary cancer. Other
 				preferred indications include
		· .		benign dysproliferative
 				disorders and pre-neoplastic
 				conditions, such as, for
				example, hyperplasia,
 				metaplasia, and/or dysplasia.
				Preferred indications include
 -				anemia, pancytopenia,
 •				leukopenia, thrombocytopenia,
			•	Hodgkin's disease, acute
 				lymphocytic anemia (ALL),
				plasmacytomas, multiple
				myeloma, Burkitt's lymphoma,
				arthritis, AIDS, granulomatous
 				disease, inflammatory bowel
 				disease, neutropenia,
 				neutrophilia, psoriasis,
 				suppression of immune
				reactions to transplanted
 				organs and tissues,
				hemophilia, hypercoagulation,
 				diabetes mellitus, endocarditis,
 				meningitis, Lyme Disease,
				cardiac reperfusion injury, and

		,			asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").
310	HLWAE11	1258	IL-10 in Human T-cell 2B9		
	HLWAE11	1258	Production of	Assays for measuring	Highly preferred indications
310			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
		((such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
				expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
				the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
	**			cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
		-	,	functions that include, but are	and/or "Cardiovascular
	-			not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
·				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,

			endothelial cells (HUVEC), which are available from commercial sources. The expression of VCAM (CD106), a membrane-associated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
HLWAE11	1258	Activation of transcription through NFKB response element in immune cells (such as natural killer cells).	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFKB transcription factors and modulate expression of immunomodulatory genes. Exemplary assays for transcription through the NFKB response element that	Highly preferred indications include inflammation and inflammatory disorders. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), and immunodeficiencies (e.g., as

may be used or rountinely modified to test NFKB-response element activity of
polypeptides of the invention (including antibodies and
agonists or antagonists of the invention) include assays
disclosed in Berger et al., Gene
66:1-10 (1998); Cullen and Malm Methods in Francol
216:362-368 (1992); Henthorn
et al., Proc Natl Acad Sci USA
85:6342-6346 (1988); Valle
Blazquez et al, Immunology
90(3):455-460 (1997);
Aramburau et al., J Exp Med
82(3):801-810 (1995); and
Fraser et al., 29(3):838-844
(1999), the contents of each of
which are herein incorporated
by reference in its entirety.
NK cells that may be used
according to these assays are
publicly available (e.g.,
through the ATCC),
Exemplary human NK cells
that may be used according to
these assays include the NKL
cell line, which is a human
natural killer cell line
established from the peripheral

			blood of a patient with large granular lymphocytic leukemia. This IL-2 dependent suspension culture cell line has a morphology resembling that of activated NK cells.	lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
HLWAE11	1258	IL-8 in SW480		Spans, worming and and Ed.
HLWAE11	1258	Calcium flux in immune cells (such	Assays for measuring calcium flux are well-known in the art	Preferred embodiments of the invention include using
		as monocytes)	and may be used or routinely modified to assess the ability	polypeptides of the invention
			of polypeptides of the	antagonists thereof) in
			invention (including antibodies	detection, diagnosis,
			and agonists or antagonists of	prevention, and/or treatment of
			calcium. Cells normally have	Atherosclerosis,
			very low concentrations of	Hypersensitivity, and
			cytosolic calcium compared to	Leukemias
			much higher extracellular	
	-		calcium. Extracellular factors	
			can cause an influx of calcium,	
			leading to activation of	
			calcium responsive signaling	

	A highly preferred embodiment of the invention includes a method for	stimulating (e.g., increasing)
pathways and alterations in cell functions. Exemplary assays that may be used or routinely modified to measure calcium flux in immune cells (such as monocytes) include assays disclosed in: Chan, CC, et al., J Pharmacol Exp Ther, 269(3):891-896 (1994); Andersson, K, et al., Cytokine, 12(12):1784-1787 (2000); Scully, SP, et al., J Clin Invest, 74(2) 589-599 (1984); and, Sullivan, E, et al., Methods Mol Biol, 114:125-133 (1999), the contents of each of which is herein incorporated by reference in its entirety. Cells that may be used according to these assays are publicly available (e.g., through the ATCC) and/or may be routinely generated. Exemplary cells that may be used according to these assays include the THP-1 monocyte cell line.	MCP-1 FMAT. Assays for immunomodulatory proteins that are produced by a large	variety of cells and act to
	Production of MCP-1	
	1259	
	HLWA022	
	311	

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MCP-1 production. An alternative highly preferred embodiment of the invention includes a method for	inhibiting (e.g., reducing) MCP-1 production. A highly preferred indication is	infection (e.g., an infectious disease as described below under "Infectious Disease").	Additional fightly preferred indications include inflammation and	inflammatory disorders. Preferred indications include	blood disorders (e.g., as described below under	"Immune Activity", "Blood-Related Disorders", and/or	"Cardiovascular Disorders"). Highly preferred indications	include autoimmune diseases (e.g., rheumatoid arthritis,	systemic lupus erythematosis, multiple sclerosis and/or as	described below) and immunodeficiencies (e.g., as	described below). Preferred	anemia, pancytopenia,	leukopenia, thrombocytopenia,
induce chemotaxis and activation of monocytes and T cells are well known in the art and may be used or routinely	modified to assess the ability of polypeptides of the invention (including antibodies	and agonists or antagonists of the invention) to mediate immunomodulation, induce	chemotaxis, and modulate immune cell activation. Exemplary assays that test for	immunomodulatory proteins evaluate the production of cell	surface markers, such as monocyte chemoattractant	protein (MCP), and the activation of monocytes and T	cells. Such assays that may be used or routinely modified to	test immunomodulatory and diffferentiation activity of	polypeptides of the invention (including antibodies and	agonists or antagonists of the invention) include assays	disclosed in Miraglia et al., J	204(1999); Rowland et al.,	"Lymphocytes: a practical
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Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple	arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia,		organs and ussues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis,	meningitis (bacterial and viral), Lyme Disease, asthma,	and allergy Preferred indications also include	neoplastic diseases (e.g., leukemia, lymphoma, and/or as	described below under "Hyperproliferative	Disorders"). Highly preferred indications include neoplasms	and cancers, such as, leukemia,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	benign dysproliferative	disorders and pre-neoplastic
approach" Chapter 6:138-160 (2000); Satthaporn and Eremin, J R Coll Surg Ednb 45(1):9-19 (2001); and	Verhasselt et al., J Immunol 158:2919-2925 (1997), the contents of each of which are	herein incorporated by reference in its entirety. Human dendritic cells that may	assays may be isolated using techniques disclosed herein or	otherwise known in the art. Human dendritic cells are	antigen presenting cells in suspension culture, which,	when activated by antigen and/or cytokines, initiate and	upregulate I cell proliteration and functional activities.				-:			
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					conditions, such as, for
					example, hyperplasia, metaplasia, and/or dysplasia.
311	HLWA022	1259	IL-10 in Human T- cell 2B9		
	HLWA022	1259	Activation of	Assays for the activation of	Highly preferred indications
311			transcription	transcription through the	include blood disorders (e.g.,
	,		through NFAT	Nuclear Factor of Activated T	as described below under
			response in immune	cells (NFAT) response element	"Immune Activity", "Blood-
			cells (such as T-	are well-known in the art and	Related Disorders", and/or
			cells).	may be used or routinely	"Cardiovascular Disorders").
				modified to assess the ability	Highly preferred indications
				of polypeptides of the	include autoimmune diseases
				invention (including antibodies	(e.g., rheumatoid arthritis,
				and agonists or antagonists of	systemic lupus erythematosis,
				the invention) to regulate	multiple sclerosis and/or as
		-		NFAT transcription factors and	described below),
				modulate expression of genes	immunodeficiencies (e.g., as
				involved in	described below), boosting a T
				immunomodulatory functions.	cell-mediated immune
				Exemplary assays for	response, and suppressing a T
				transcription through the	cell-mediated immune
				NFAT response element that	response. Additional highly
				may be used or routinely	preferred indications include
				modified to test NFAT-	inflammation and
				response element activity of	inflammatory disorders. An
-				polypeptides of the invention	additional highly preferred
				(including antibodies and	indication is infection (e.g., an
				agonists or antagonists of the	infectious disease as described
				invention) include assays	below under "Infectious
				disclosed in Berger et al., Gene	Disease"). Preferred

		66:1-10 (1998): Cullen and	indications include neoplastic
		Malm. Methods in Enzymol	diseases (e.g., leukemia.
		216:362-368 (1992); Henthorn	lymphoma, and/or as described
		et al., Proc Natl Acad Sci USA	below under
		85:6342-6346 (1988); Serfling	"Hyperproliferative
		et al., Biochim Biophys Acta	Disorders"). Preferred
		1498(1):1-18 (2000); De Boer	indications include neoplasms
		et al., Int J Biochem Cell Biol	and cancers, such as, for
		31(10):1221-1236 (1999);	example, leukemia, lymphoma,
	7	Fraser et al., Eur J Immunol	and prostate, breast, lung,
		29(3):838-844 (1999); and	colon, pancreatic, esophageal,
		Yeseen et al., J Biol Chem	stomach, brain, liver and
		268(19):14285-14293 (1993),	urinary cancer. Other preferred
		the contents of each of which	indications include benign
		are herein incorporated by	dysproliferative disorders and
		reference in its entirety. T	pre-neoplastic conditions, such
		cells that may be used	as, for example, hyperplasia,
		according to these assays are	metaplasia, and/or dysplasia.
	-	publicly available (e.g.,	Preferred indications also
		through the ATCC).	include anemia, pancytopenia,
		Exemplary human T cells that	leukopenia, thrombocytopenia,
		may be used according to these	Hodgkin's disease, acute
		assays include the JURKAT	lymphocytic anemia (ALL),
		cell line, which is a suspension	plasmacytomas, multiple
		culture of leukemia cells that	myeloma, Burkitt's lymphoma,
		produce IL-2 when stimulated.	arthritis, AIDS, granulomatous
			disease, inflammatory bowel
			disease, sepsis, neutropenia,
			neutrophilia, psoriasis,
			suppression of immune
			reactions to transplanted

					organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and allergy.
311	HLWA022	1259	Activation of transcription	Assays for the activation of transcription through the	A preferred embodiment of the invention includes a
			through serum response element in	Serum Response Element (SRE) are well-known in the	method for inhibiting (e.g., reducing) TNF alpha
			immune cells (such as natural killer	art and may be used or routinely modified to assess	production. An alternative highly preferred embodiment
			cells).	the ability of polypeptides of	of the invention includes a
				the invention (including antibodies and agonists or	method for sumulating (e.g., increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
				regulate serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth and upregulate the	Activity", "Blood-Related
				function of growth-related	Disorders", and/or
				genes in many cell types.	"Cardiovascular Disorders"),
				Exemplary assays for	Highly preferred indications
				transcription through the SRE	include autoimmune diseases
				that may be used or routinely	(e.g., rheumatoid arthritis,
				modified to test SRE activity	systemic lupus erythematosis,
				of the polypeptides of the	Crohn"s disease, multiple
				invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below), immunodeficiencies
				the invention) include assays	(e.g., as described below),
				disclosed in Berger et al., Gene	boosting a T cell-mediated
		 		66:1-10 (1998); Cullen and	immune response, and

suppressing a T cell-mediated immune response. Additional highly preferred indications include inflammation and inflammatory disorders, and	treating joint damage in patients with rheumatoid arthritis. An additional highly preferred indication is sepsis. Highly preferred indications include neoplastic diseases (e.g., leukemia, lymnhoma	and/or as described below under "Hyperproliferative Disorders"). Additionally, highly preferred indications include neoplasms and cancers, such as, for example, leukemia, lymphoma, melanoma, glioma (e.g.,	malignant glioma), solid tumors, and prostate, breast, lung, colon, pancreatic, esophageal, stomach, brain, liver and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.
Malm, Methods in Enzymol 216:362-368 (1992); Henthorn et al., Proc Natl Acad Sci USA 85:6342-6346 (1988); Benson et al., J Immunol 153(9):3862-3873 (1904); and Black et al.	Virus Genes 12(2):105-117 (1997), the content of each of which are herein incorporated by reference in its entirety. T cells that may be used according to these assays are	publicly available (e.g., through the ATCC). Exemplary T cells that may be used according to these assays include the NK-YT cell line, which is a human natural killer cell line with cytolytic and cytotoxic activity.	

					Preferred indications include
					anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					arthritis, AIDS, granulomatous
					disease, inflammatory bowel
					disease, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues, hemophilia,
					hypercoagulation, diabetes
					mellitus, endocarditis,
				_	meningitis, Lyme Disease,
					cardiac reperfusion injury, and
					asthma and allergy. An
					additional preferred indication
					is infection (e.g., an infectious
					disease as described below
					under "Infectious Disease").
	HLWAY54	1260	Production of	MCP-1 FMAT. Assays for	A highly preferred
312			MCP-1	immunomodulatory proteins	embodiment of the invention
				that are produced by a large	includes a method for
				variety of cells and act to	stimulating (e.g., increasing)
				induce chemotaxis and	MCP-1 production. An
				activation of monocytes and T	alternative highly preferred
				cells are well known in the art	embodiment of the invention
				and may be used or routinely	includes a method for

modified to assess the ability		inhibiting (e.g., reducing)
of polypeptides of the		MCP-1 production. A highly
invention (including antibodies		IS.
and agonists or antagonists of		infection (e.g., an infectious
the invention) to mediate		disease as described below
immunomodulation, induce		under "Infectious Disease").
chemotaxis, and modulate		Additional highly preferred
immune cell activation.	- in	indications include
Exemplary assays that test for		inflammation and
 immunomodulatory proteins		inflammatory disorders.
 evaluate the production of cell	=	Preferred indications include
surface markers, such as		blood disorders (e.g., as
 monocyte chemoattractant		described below under
protein (MCP), and the	<u>I,,</u>	"Immune Activity", "Blood-
activation of monocytes and T		Related Disorders", and/or
cells. Such assays that may be		"Cardiovascular Disorders").
used or routinely modified to		Highly preferred indications
 test immunomodulatory and		include autoimmune diseases
differentiation activity of	-	(e.g., rheumatoid arthritis,
polypeptides of the invention		systemic lupus erythematosis,
(including antibodies and		multiple sclerosis and/or as
agonists or antagonists of the		described below) and
 invention) include assays	-	immunodeficiencies (e.g., as
disclosed in Miraglia et al., J	_	described below). Preferred
Biomolecular Screening 4:193-	193-	indications also include
 204(1999); Rowland et al.,		anemia, pancytopenia,
"Lymphocytes: a practical		leukopenia, thrombocytopenia,
 approach" Chapter 6:138-160		Hodgkin's disease, acute
(2000); Satthaporn and		lymphocytic anemia (ALL),
 Eremin, J R Coll Surg Ednb		plasmacytomas, multiple
45(1):9-19 (2001); and	m	myeloma, Burkitt's lymphoma,

			Verhasselt et al., J Immunol	arthritis, AIDS, granulomatous
			158:2919-2925 (1997), the	disease, inflammatory bowel
			contents of each of which are	disease, sepsis, neutropenia,
			herein incorporated by	neutrophilia, psoriasis,
			reference in its entirety.	suppression of immune
			Human dendritic cells that may	reactions to transplanted
			be used according to these	organs and tissues,
			assays may be isolated using	hemophilia, hypercoagulation,
			techniques disclosed herein or	diabetes mellitus, endocarditis,
			otherwise known in the art.	meningitis (bacterial and
			Human dendritic cells are	viral), Lyme Disease, asthma,
			antigen presenting cells in	and allergy Preferred
			suspension culture, which,	indications also include
			when activated by antigen	neoplastic diseases (e.g.,
			and/or cytokines, initiate and	leukemia, lymphoma, and/or as
			upregulate T cell proliferation	described below under
			and functional activities.	"Hyperproliferative
				Disorders"). Highly preferred
				indications include neoplasms
				and cancers, such as, leukemia,
				lymphoma, prostate, breast,
				lung, colon, pancreatic,
				esophageal, stomach, brain,
				liver, and urinary cancer. Other
				preferred indications include
				benign dysproliferative
4				disorders and pre-neoplastic
				conditions, such as, for
				example, hyperplasia,
				metaplasia, and/or dysplasia.
HLWAY54	1260	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications

include asthma allerov					indications include immune		(e.g., as described below under		"Blood-Related Disorders"),	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, Crohn"s	disease, multiple sclerosis	and/or as described below),	immunodeficiencies (e.g., as		es preferred indications also	f include boosting or inhibiting	immune cell proliferation.	Preferred indications include	- neoplastic diseases (e.g.,	p leukemia, lymphoma, and/or as		n "Hyperproliferative	Disorders"). Highly preferred	indications include boosting an	eosinophil-mediated immune	l response, and suppressing an		
assays for signal transduction	that regulate cell proliferation.	activation, or apoptosis are	well known in the art and may	be used or routinely modified	to assess the ability of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) to promote or	inhibit cell proliferation,	activation, and apoptosis.	Exemplary assays for JNK	kinase activity that may be	used or routinely modified to	test JNK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Gupta et al., Exp	Cell Res 247(2): 495-504	(1999); Kyriakis JM, Biochem	Soc Symp 64:29-48 (1999);	Chang and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	
Signaling Pathway	in immune cells	(such as	eosinophils).															-				-								
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312															19															_

are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;	Oct;122(1):20-7 (2000);
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				Hebestreit H. et al	
				"Disruption of fas receptor	
				signaling by nitric oxide in	
				eosinophils" J Exp Med; Feb	
	~			2;187(3):415-25 (1998); J	
				Allergy Clin Immunol 1999	
				Sep;104(3 Pt 1):565-74; and,	
				Sousa AR, et al., "In vivo	
				resistance to corticosteroids in	
				bronchial asthma is associated	
				with enhanced	
				phosyphorylation of JUN N-	
	,			terminal kinase and failure of	
				prednisolone to inhibit JUN N-	
				terminal kinase	
				phosphorylation" J Allergy	
				Clin Immunol; Sep;104(3 Pt	
				1):565-74 (1999); the contents	
				of each of which are herein	
				incorporated by reference in its	
				entirety.	
	HLWAY54	1260	SEAP in		
312			HepG2/Squale-		
			synthetase(stimulati		
	HI WAVSA	1260	CD152 in Human T		
312	11LWA134	1700	cells		
	HLWAY54	1260	SEAP in OE-33		
312					
	HLWAY54	1260	SEAP in		
312			Senescence Assay		

	HLWBH18	1261	Inhibition of	Reporter Assay: construct	
313			squalene synthetase	contains regulatory and coding	
			gene transcription.	sequence of squalene	
				synthetase, the first specific	
				enzyme in the cholesterol	
			-	biosynthetic pathway. See	
				Jiang, et al., J. Biol. Chem.	
				268:12818-128241(993), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety. Cells were treated	
				with SID supernatants, and	
				SEAP activity was measured	
				after 72 hours. HepG2 is a	
				human hepatocellular	
				carcinoma cell line (ATCC	
				HB-8065). See Knowles et al.,	
				Science. 209:497-9 (1980), the	
				contents of which are herein	
				incorporated by reference in its	
				entirety.	
	HLWBH18	1261	Activation of	Kinase assay. JNK and p38	A highly preferred
313			Endothelial Cell	kinase assays for signal	embodiment of the invention
			p38 or JNK	transduction that regulate cell	includes a method for
			Signaling Pathway.	proliferation, activation, or	stimulating endothelial cell
				apoptosis are well known in	growth. An alternative highly
				the art and may be used or	preferred embodiment of the
				routinely modified to assess	invention includes a method
				the ability of polypeptides of	for inhibiting endothelial cell
				the invention (including	growth. A highly preferred
				antibodies and agonists or	embodiment of the invention

	antanonists of the invention) to includes a method for	includes a method for
	and solution of the meaning to	etimuloting andotholist coll
	promote or minot cen	sumulating endotherial cell
	proliferation, activation, and	proliferation. An alternative
	apoptosis. Exemplary assays	highly preferred embodiment
	for JNK and p38 kinase	of the invention includes a
	activity that may be used or	method for inhibiting
	routinely modified to test JNK	endothelial cell proliferation.
	and p38 kinase-induced	A highly preferred
	activity of polypeptides of the	embodiment of the invention
	invention (including antibodies	includes a method for
	and agonists or antagonists of	stimulating apoptosis of
	the invention) include the	endothelial cells. An
	assays disclosed in Forrer et	alternative highly preferred
	al., Biol Chem 379(8-9):1101-	embodiment of the invention
	1110 (1998); Gupta et al., Exp	includes a method for
	Cell Res 247(2): 495-504	inhibiting (e.g., decreasing)
	(1999); Kyriakis JM, Biochem	apoptosis of endothelial cells.
	Soc Symp 64:29-48 (1999);	A highly preferred
	Chang and Karin, Nature	embodiment of the invention
	410(6824):37-40 (2001); and	includes a method for
	Cobb MH, Prog Biophys Mol	stimulating (e.g., increasing)
	Biol 71(3-4):479-500 (1999);	endothelial cell activation. An
	the contents of each of which	alternative highly preferred
	are herein incorporated by	embodiment of the invention
	reference in its entirety.	includes a method for
	Endothelial cells that may be	inhibiting (e.g., decreasing) the
	used according to these assays	activation of and/or
	are publicly available (e.g.,	inactivating endothelial cells.
	through the ATCC).	A highly preferred
	Exemplary endothelial cells	embodiment of the invention
	that may be used according to	includes a method for

as described below under	"Cardiovascular Disorders").	Highly preferred indications	include cardiovascular,	endothelial and/or angiogenic	disorders (e.g., systemic	disorders that affect vessels	such as diabetes mellitus, as	well as diseases of the vessels	themselves, such as of the	arteries, capillaries, veins	and/or lymphatics). Highly	preferred are indications that	stimulate angiogenesis and/or	cardiovascularization. Highly	preferred are indications that	inhibit angiogenesis and/or	cardiovascularization.	Highly preferred indications	include antiangiogenic activity	to treat solid tumors,	leukemias, and Kaposi"s	sarcoma, and retinal disorders.	Highly preferred indications	include neoplasms and cancer,	such as, Kaposi's sarcoma,	hemangioma (capillary and	cavernous), glomus tumors,	telangiectasia, bacillary	angiomatosis,	hemangioendothelioma,
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angiosarcoma, haemanoionericytoma	lymphangioma,	lymphangiosarcoma. Highly	preferred indications also	include cancers such as,	prostate, breast, lung, colon,	pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	Highly preferred indications	also include arterial disease,	such as, atherosclerosis,	hypertension, coronary artery	disease, inflammatory	vasculitides, Reynaud"s	disease and Reynaud"s	phenomenom, aneurysms,	restenosis; venous and	lymphatic disorders such as	thrombophlebitis,	lymphangitis, and	lymphedema; and other	vascular disorders such as	peripheral vascular disease,	and cancer. Highly
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preferred indications also	include trauma such as	wounds, burns, and injured	tissue (e.g., vascular injury	such as, injury resulting from	balloon angioplasty, and	atheroschlerotic lesions),	implant fixation, scarring,	ischemia reperfusion injury,	rheumatoid arthritis,	cerebrovascular disease, renal	diseases such as acute renal	failure, and osteoporosis.	Additional highly preferred	indications include stroke,	graft rejection, diabetic or	other retinopathies, thrombotic	and coagulative disorders,	vascularitis, lymph	angiogenesis, sexual disorders,	age-related macular	degeneration, and treatment	/prevention of endometriosis	and related conditions.	Additional highly preferred	indications include fibromas,	heart disease, cardiac arrest,	heart valve disease, and	vascular disease.	Preferred indications include	blood disorders (e.g., as
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					described below under
					"Immune Activity", "Blood-
					Related Disorders", and/or
					"Cardiovascular Disorders").
					Preferred indications include
					autoimmune diseases (e.g.,
					rheumatoid arthritis, systemic
					lupus erythematosis, multiple
					sclerosis and/or as described
					below) and
					immunodeficiencies (e.g., as
					described below). Additional
					preferred indications include
					inflammation and
					inflammatory disorders (such
					as acute and chronic
					inflammatory diseases, e.g.,
					inflammatory bowel disease
					and Crohn's disease), and pain
					management.
313	HLWBH18	1261	SEAP in OE-33		
314	HLWBI63	1262	CD71 in Human T cells		
	HLWBK05	1263	Activation of	Kinase assay. Kinase assays,	A highly preferred
315			Adipocyte ERK	for example an Elk-1 kinase	embodiment of the invention
			Signaling Pathway	assay, for ERK signal	includes a method for
				transduction that regulate cell	stimulating adipocyte
				proliferation or differentiation	proliferation. An alternative
				are well known in the art and	highly preferred embodiment
				may be used or routinely	of the invention includes a

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mothod for inhihiting		adipocyte proliferation. A	highly preferred embodiment	of the invention includes a	method for stimulating	adipocyte differentiation. An	alternative highly preferred	embodiment of the invention	includes a method for	inhibiting adipocyte	differentiation. A highly	preferred embodiment of the	invention includes a method	for stimulating (e.g.,	increasing) adipocyte	activation. An alternative	highly preferred embodiment	of the invention includes a	method for inhibiting the	activation of (e.g., decreasing)	and/or inactivating adipocytes.	Highly preferred indications	include endocrine disorders	(e.g., as described below under	"Endocrine Disorders").	Highly preferred indications	also include neoplastic	diseases (e.g., lipomas,	liposarcomas, and/or as	described below under	J.1.
modified to energy the ability	illouilled to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to promote or	inhibit cell proliferation,	activation, and differentiation.	Exemplary assays for ERK	kinase activity that may be	used or routinely modified to	test ERK kinase-induced	activity of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in Forrer et	al., Biol Chem 379(8-9):1101-	1110 (1998); Le Marchand-	Brustel Y, Exp Clin	Endocrinol Diabetes	107(2):126-132 (1999);	Kyriakis JM, Biochem Soc	Symp 64:29-48 (1999); Chang	and Karin, Nature	410(6824):37-40 (2001); and	Cobb MH, Prog Biophys Mol	Biol 71(3-4):479-500 (1999);	the contents of each of which	are herein incorporated by	reference in its entirety.	
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Disorders"). Preferred indications include blood disorders (e.g., hypertension,	vessel blockage, heart disease, stroke, impotence and/or as described below under	"Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related	(e.g., as described below under "Immune Activity"), neural	disorders (e.g., as described below under "Neural Activity	and Neurological Diseases"),	and infection (e.g., as described below under	"Infectious Disease").	ndica	is diabetes mellitus. An additional highly preferred	indication is a complication	associated with diabetes (e.g., diabetic retinopathy, diabetic	nephropathy, kidney disease	(e.g., renal failure,	nephropathy and/or other	diseases and disorders as	described in the "Renal	Disorders" section below),
se	cells that may be used according to these assays include 3T3-L1 cells 3T3-L1		pu	der	ن	<u>в</u>	77	7	11 - 8		8 0	<u> </u>)	p	
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diabetic neuropathy, nerve disease and nerve damage (e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke,	impotence (e.g., due to diabetic neuropathy or blood vessel blockage), seizures, mental	nonketotic hyperglycemichyperosmolar coma,	heart disease, atherosclerosis,	hypertension, stroke, and other diseases and disorders as	described in the "Cardiovascular Disorders"	section below), dyslipidemia, endocrine disorders (as	described in the "Endocrine Disorders" section below),	neuropathy, vision impairment (e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g., infections diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the urinary tract and skin). An
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	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred	indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Preferred	indications include neoplasms	and cancer, such as,	lymphoma, leukemia and	breast, colon, and kidney	cancer. Additional preferred	indications include melanoma,
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					prostate, lung, pancreatic,
					esophageal, stomach, brain,
					liver, and urinary cancer.
					Highly preferred indications
					include lipomas and
					liposarcomas. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
Ţ.	HLWBY76	1264	Activation of	Assays for the activation of	A preferred embodiment of
316			transcription	transcription through the	the invention includes a
			through serum	Serum Response Element	method for inhibiting (e.g.,
			response element in	(SRE) are well-known in the	reducing) TNF alpha
			immune cells (such	art and may be used or	production. An alternative
			as T-cells).	routinely modified to assess	preferred embodiment of the
				the ability of polypeptides of	invention includes a method
				the invention (including	for stimulating (e.g.,
				antibodies and agonists or	increasing) TNF alpha
				antagonists of the invention) to	production. Preferred
·				regulate the serum response	indications include blood
				factors and modulate the	disorders (e.g., as described
				expression of genes involved	below under "Immune
				in growth. Exemplary assays	Activity", "Blood-Related
				for transcription through the	Disorders", and/or
		71		SRE that may be used or	"Cardiovascular Disorders"),
				routinely modified to test SRE	Highly preferred indications
				activity of the polypeptides of	include autoimmune diseases
				the invention (including	(e.g., rheumatoid arthritis,
				antibodies and agonists or	systemic lupus erythematosis,

		antagonists of the invention)	Crohn"s disease, multiple
	-	include assays disclosed in	sclerosis and/or as described
		Berger et al., Gene 66:1-10	below), immunodeficiencies
		(1998); Cullen and Malm,	(e.g., as described below),
		Methods in Enzymol 216:362-	boosting a T cell-mediated
		368 (1992); Henthorn et al.,	immune response, and
		Proc Natl Acad Sci USA	suppressing a T cell-mediated
		85:6342-6346 (1988); and	immune response. Additional
		Black et al., Virus Genes	highly preferred indications
	-	12(2):105-117 (1997), the	include inflammation and
		content of each of which are	inflammatory disorders, and
		herein incorporated by	treating joint damage in
		reference in its entirety. T	patients with rheumatoid
-		cells that may be used	arthritis. An additional highly
		according to these assays are	preferred indication is sepsis.
		publicly available (e.g.,	Highly preferred indications
		through the ATCC).	include neoplastic diseases
		Exemplary mouse T cells that	(e.g., leukemia, lymphoma,
		may be used according to these	and/or as described below
		assays include the CTLL cell	under "Hyperproliferative
	-	line, which is an IL-2	Disorders"). Additionally,
		dependent suspension culture	highly preferred indications
		of T cells with cytotoxic	include neoplasms and
		activity.	cancers, such as, for example,
			leukemia, lymphoma,
			melanoma, glioma (e.g.,
			malignant glioma), solid
			tumors, and prostate, breast,
			lung, colon, pancreatic,
			esophageal, stomach, brain,
			liver and urinary cancer. Other

			prefer	preferred indications include
			benig	benign dysproliferative
			disord	disorders and pre-neoplastic
	-		condi	conditions, such as, for
·····			exam	example, hyperplasia,
			meta	metaplasia, and/or dysplasia.
			Prefe	Preferred indications include
			anem	anemia, pancytopenia,
			leuko	leukopenia, thrombocytopenia,
			Hodg	Hodgkin's disease, acute
			lympl	lymphocytic anemia (ALL),
			plasm	plasmacytomas, multiple
			myele	myeloma, Burkitt's lymphoma,
			arthri	arthritis, AIDS, granulomatous
			diseas	disease, inflammatory bowel
			diseas	disease, neutropenia,
			neutr	neutrophilia, psoriasis,
			zddns	suppression of immune
			reacti	reactions to transplanted
			organ	organs and tissues,
			hemo	hemophilia, hypercoagulation,
		-	diabe	diabetes mellitus, endocarditis,
			menir	meningitis, Lyme Disease,
			cardie	cardiac reperfusion injury, and
			asthm	asthma and allergy. An
			additi	additional preferred indication
			is infe	is infection (e.g., an infectious
	-11-21-		diseas	disease as described below
			nnder	under "Infectious Disease").
HLWBY76	1264	CD152 in Human T		

	HI WRV76	1264	HI A. DR in Himan		
316		· · · · · · · · · · · · · · · · · · ·	T cells		
	HLWCF05	1265	Activation of	Kinase assay. Kinase assays,	A highly preferred
317			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
				survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method
· · · ·				antibodies and agonists or	for stimulating adipocyte
				antagonists of the invention) to	proliferation. An alternative
				promote or inhibit glucose	highly preferred embodiment
				metabolism and cell survival.	of the invention includes a
				Exemplary assays for PI3	method for inhibiting
				kinase activity that may be	adipocyte proliferation. A
				used or routinely modified to	preferred embodiment of the
			-	test PI3 kinase-induced activity	invention includes a method
				of polypeptides of the	for stimulating adipocyte
				invention (including antibodies	differentiation. An alternative
				and agonists or antagonists of	highly preferred embodiment
				the invention) include assays	of the invention includes a
				disclosed in Forrer et al., Biol	method for inhibiting
				Chem 379(8-9):1101-1110	adipocyte differentiation.
				(1998); Nikoulina et al.,	Highly preferred indications
				Diabetes 49(2):263-271	include endocrine disorders
				(2000); and Schreyer et al.,	(e.g., as described below under
				Diabetes 48(8):1662-1666	"Endocrine Disorders").
				(1999), the contents of each of	Preferred indications include

		which are herein incorporated	neoplastic diseases (e.g.,
		by reference in its entirety.	linomas linosarcomas and/or
	-	Mouse adinocyte cells that	as described below under
		may be used according to these	"Hyperproliferative
	-	assays are publicly available	Disorders"), blood disorders
		(e.g., through the ATCC).	(e.g., hypertension, congestive
		Exemplary mouse adipocyte	heart failure, blood vessel
		cells that may be used	blockage, heart disease, stroke,
		according to these assays	impotence and/or as described
		include 3T3-L1 cells. 3T3-L1	below under "Immune
		is an adherent mouse	Activity", "Cardiovascular
		preadipocyte cell line that is a	Disorders", and/or "Blood-
-		continous substrain of 3T3	Related Disorders"), immune
	 	fibroblast cells developed	disorders (e.g., as described
		through clonal isolation and	below under "Immune
		undergo a pre-adipocyte to	Activity"), neural disorders
		adipose-like conversion under	(e.g., as described below under
		appropriate differentiation	"Neural Activity and
		conditions known in the art.	Neurological Diseases"), and
			infection (e.g., as described
			below under "Infectious
	 		Disease"). A highly
			preferred indication is diabetes
			mellitus. An additional
			highly preferred indication is a
			complication associated with
			diabetes (e.g., diabetic
			retinopathy, diabetic
			nephropathy, kidney disease
			(e.g., renal failure,
			nephropathy and/or other

diseases and disorders as described in the "Renal	Disorders" section below),	diabetic neuropathy, nerve	disease and nerve damage (e.g.	due to diabetic neuropathy),	blood vessel blockage, heart	disease, stroke, impotence	(e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	discorders as described in the
														•														-	
									,											-	-				•				

urinary tact and skin), tunnel syndrome and Dupuytra is contractud obesity. Additional highly preferred indications associating weight loss or alternatic weight gain. Additional highly preferred indications associated insulin resistance. Additional highly preferred indications as disorde musculoskeletal system including myopathies, muscular dystrophy, at described herein. Additional highly preferred indications are disorde indications included indications included indications, osconary disease, dyslipidemia, gallstones, osteoarthrif degenerative arthrifts, disorders. Highly preferred indications included indications in ind			"Infectious Diseases" section
unmal syndrome and Dupuytren's contract An additional highly indication is obesity a complications associo obesity. Additional highly indications associi obesity. Additional syndrome weight loss or alternate weight loss or alternate or a complications associi insulin resistance. Additional highly preferred indications associi insulin resistance. Additional highly preintifications are discording myopathic musculas dystrophy, described herein. Additional highly preintifications are discording myopathic misclations include, hypertension, corona disease, dyslipidemii gallstones, osteoarthic degenerative arthritifications includes, highly preintifications include, hypertension, corona disease, dyslipidemii gallstones, osteoarthic discorders. Highly insuline sitemates, discorders, filthy insuline sitemates, discorders, filthy discorders, discorders, filthy discorders, discorders.			below, especially of the
umnel syndrome and Dupuytren's contract An additional highly indication is obesity a complications associo obesity. Additional I preferred indications associo insight gain. A highly preferred indications associo insight preferred indications associo insight preferred indications associo insight preferred indications are disorded in the complications are disorded in the complex of the complex o			urinary tract and skin), carpal
Dupuytren's contract An additional highly indication is obesity indication is obesity. Additional preferred indications sweight loss or alterna weight gain. A highly preferred indications association insulin resistance. Additional highly preinculous proceeds a specific musculoskeletal systic including myopathic musculoskeletal systic including myopathic musculoskeletal systic including myopathic described herein. Additional highly preinciple include, hypertension, corona disease, dyslipiemic gallstones, osteoarthin degenerative arthritis disorders, fibrosis, cand kidney diseases disorders. Highly indirections are discorders. Highly indirections includes disorders.			tunnel syndrome and
An additional highly indication is obesity complications associt obesity complications associt obesity additional preferred indications weight loss or alterne weight gain. In highly preferred indications associt insulin resistance. Additional highly pre indications are disord musculoskeletal systimation in the companient distribution myopathie. Additional highly pre indications include, hypertension, corona disease, dyslipidemitic gallstones, osteoarthy degenerative arthritic disorders, fibrosis, cand kidney diseases disorders. Highly indications includes indications includes disorders, fibrosis, candidations includes disorders. Highly instinctes.			Dupuytren's contracture).
indication is obesity a complications associo obesity. Additional P preferred indications weight loss or alternate weight loss or alternate weight gain. Additional highly preferred indications associon insulin resistance. Additional highly preinted discrete discrete musculoskeletal systimicluding myopathies. Maditional highly preinted indications include, hypertension, coronal disease, dyslipidemitic gallstones, ostocoarthy degenerative arthritis disorders, fibrosis, or and kidney diseases disorders. Highly indications includes indications includes indications diseases disorders. Highly indications includes indications in indications indications indications indications indications indications indic			An additional highly preferred
complications associ obesity. Additional Preferred indications weight loss or alternate weight loss or alternate weight loss or alternate weight gain. Weight preferred indications associinsulin resistance. Additional highly preinfluid myopathics muscular dystrophy, described herein. Additional highly preinfluid highly preinfluid myopathics including myopathics indications include, hypertension, coronate disease, dyslipidemic gallstones, osteoarthy degenerative arthritis disorders. Highly indications in disorders. Highly indications in the disorders.		-	indication is obesity and/or
obesity. Additional preferred indications weight loss or alterna weight gain. Weight loss or alterna weight gain. Additional highly preferred indications associansulin resistance. Additional highly praindications are disord muscular dystrophy, described herein. Additional highly praindications include, hypertension, corona disease, dyslipidemic gallstones, osteoarth degenerative arthritis disorders, fibrosis, or and kidney diseases disorders. Highly indications include, indications include, indications.			complications associated with
preferred indications weight loss or alterna weight gain. highly preferred indic complications associ insulin resistance. Additional highly pre including myopathic muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, ca and kidney diseases disorders. Highly indications include, disorders, fibrosis, ca and kidney diseases disorders. Highly			obesity. Additional highly
weight loss or alterna weight gain. A highly preferred indic complications associa insulin resistance. Additional highly pre indications are disore musculoskeletal syst including myopathic muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthu degenerative arthritis disorders, fibrosis, or and kidney diseases disorders. Highly indications: Highly indicorders. Highly indicorders. Highly indicorders. Highly indicorders. Highly			preferred indications include
weight gain. A highly preferred indicomplications associa insulin resistance. Additional highly pre indications are disord musculoskeletal system including myopathics muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthic degenerative arthritic disorders, fibrosis, cand disorders, fibrosis, cand resistance in disorders. Highly disorders. Highly disorders. Highly disorders.			weight loss or alternatively,
highly preferred indicomplications associal insulin resistance. Additional highly pre indications are disord musculoskeletal system including myopathics muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthic degenerative arthritic disorders, fibrosis, or and kidney diseases a disorders. Highly highly disorders. Highly highly disorders.			weight gain. Additional
complications associ insulin resistance. Additional highly pre indications are disord musculoskeletal syst including myopathie: muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthic disorders, fibrosis, cand kidney diseases idisorders. Highly described in disorders. Highly described in disorders. Highly disorders.			highly preferred indications are
Additional highly pre indications are disorc musculoskeletal systi including myopathic: muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, c and kidney diseases i disorders. Highly			complications associated with
Additional highly pre indications are disore musculoskeletal syste including myopathies muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarth degenerative arthritic disorders, fibrosis, ce and kidney diseases of disorders. Highly			insulin resistance.
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musculoskeletal syste including myopathies muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, cc and kidney diseases i disorders. Highly indications include, indications includes incl			indications are disorders of the
including myopathies muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, cs and kidney diseases a disorders. Highly			musculoskeletal systems
muscular dystrophy, described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemie gallstones, osteoarthi degenerative arthritis disorders, fibrosis, cz and kidney diseases of disorders. Highly indications include by			including myopathies,
described herein. Additional highly pre indications include, hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, cannot kidney diseases and kidney diseases disorders. Highly indications includes			muscular dystrophy, and/or as
Additional highly pre indications include, hypertension, corona disease, dyslipidemiz gallstones, osteoarthr degenerative arthritis disorders, fibrosis, cand kidney diseases disorders. Highly indications include and highly indications include and highly indications include and highly indications.			described herein.
indications include, hypertension, corona disease, dyslipidemie gallstones, osteoarthe degenerative arthritis disorders, fibrosis, ce and kidney diseases e disorders. Highly			Additional highly preferred
hypertension, corona disease, dyslipidemic gallstones, osteoarthi degenerative arthritis disorders, fibrosis, cand kidney diseases (disorders. Highly indications includes and highly indications in the hig			indications include,
disease, dyslipidemia gallstones, osteoarthr degenerative arthritis disorders, fibrosis, ce and kidney diseases of disorders. Highly			hypertension, coronary artery
gallstones, osteoarthr degenerative arthritis disorders, fibrosis, ce and kidney diseases of disorders. Highly			disease, dyslipidemia,
degenerative arthritis disorders, fibrosis, ce and kidney diseases of disorders. Highly			gallstones, osteoarthritis,
disorders, fibrosis, ca and kidney diseases of disorders. Highly indications include a			degenerative arthritis, eating
and kidney diseases of disorders. Highly indications include a			disorders, fibrosis, cachexia,
disorders. Highly			and kidney diseases or
* of it own two to the			disorders. Highly preferred
ווומוכיותם וזי	-		indications include neoplasms

					and cancer such as linoma
					tree day on the state of the st
					nposarcoma, iympnoma,
					leukemia and breast, colon,
					and kidney cancer. Additional
					highly preferred indications
					include melanoma, prostate,
					lung, pancreatic, esophageal,
					stomach, brain, liver, and
					urinary cancer. Other preferred
					indications include benign
					dysproliferative disorders and
					pre-neoplastic conditions, such
					as, for example, hyperplasia,
					metaplasia, and/or dysplasia.
	HLWCF05	1265	Activation of JNK	Kinase assay. JNK kinase	Highly preferred indications
317			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			snch as	activation, or apoptosis are	inflammation, and
			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
				invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
		į		test JNK kinase-induced	immunodeficiencies (e.g., as

activity of polypeptides of the	described below). Highly
invention (including antibodies	preferred indications also
and agonists or antagonists of	include boosting or inhibiting
the invention) include the	immune cell proliferation.
assays disclosed in Forrer et	Preferred indications include
al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
Cell Res 247(2): 495-504	described below under
(1999); Kyriakis JM, Biochem	"Hyperproliferative
Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
Chang and Karin, Nature	indications include boosting an
410(6824):37-40 (2001); and	eosinophil-mediated immune
Cobb MH, Prog Biophys Mol	response, and suppressing an
Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune
 the contents of each of which	response.
are herein incorporated by	
reference in its entirety.	
Exemplary cells that may be	
used according to these assays	
include eosinophils.	
Eosinophils are important in	
the late stage of allergic	
reactions; they are recruited to	
tissues and mediate the	
inflammatory response of late	
stage allergic reaction.	
Moreover, exemplary assays	
that may be used or routinely	
modified to assess the ability	
of polypeptides of the	
invention (including antibodies	

and agonists or antagonists of the invention) to modulate signal transduction, cell profileration, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang JP, et al., "Role of caspases in dexamethasone-induced apoptosis and activation of c-Jun NH2-terminal kinase and p38 mitogen-activated protein kinase in human eosinophils." Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils." Exp Med; Feb 2;187(3):415-25 (1998); J Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced phosyphorylation of JUN N-terminal kinase and failure of prednisolone to inhibit JUN N-terminal kinase phosphorylation." J Allergy					
	and agonists or antagonists of the invention) to modulate signal transduction, cell proliferation, activation, or apoptosis in eosinophils include assays disclosed and/or cited in: Zhang IP et al "Role cited in: Zhang IP et al "Role	of caspases in dexamethasone- induced apoptosis and activation of c-Jun NH2- terminal kinase and p38 mitogen-activated protein	kinase in human eosinophils" Clin Exp Immunol; Oct;122(1):20-7 (2000); Hebestreit H, et al., "Disruption of fas receptor signaling by nitric oxide in eosinophils" J Exp Med; Feb 2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999 Sep;104(3 Pt 1):565-74; and, Sousa AR, et al., "In vivo resistance to corticosteroids in bronchial asthma is associated with enhanced	phosyphorylation of JUN N- terminal kinase and failure of prednisolone to inhibit JUN N- terminal kinase phosphorylation" J Allergy
				-	

				Clin Imminol: Sen: 104/3 Dt	
				1):565-74 (1999); the contents of each of which are herein	
				incorporated by reference in its entirety.	
317	HLWCF05	1265	SEAP in OE-21		
317	HLWCF05	1265	SEAP in OE-33		
	HLWCF05	1265	Activation of	Assays for the activation of	Preferred indications
317			transcription	transcription through the AP1	include neoplastic diseases
			through AP1	response element are well-	(e.g., as described below under
			response element in	known in the art and may be	"Hyperproliferative
			immune cells (such	used or routinely modified to	Disorders"), blood disorders
			as T-cells).	assess the ability of	(e.g., as described below under
				polypeptides of the invention	"Immune Activity",
				(including antibodies and	"Cardiovascular Disorders",
				agonists or antagonists of the	and/or "Blood-Related
				invention) to modulate growth	Disorders"), and infection
				and other cell functions.	(e.g., an infectious disease as
				Exemplary assays for	described below under
	4			transcription through the AP1	"Infectious Disease"). Highly
				response element that may be	preferred indications include
				used or routinely modified to	autoimmune diseases (e.g.,
				test AP1-response element	rheumatoid arthritis, systemic
-		277.44		activity of polypeptides of the	lupus erythematosis, multiple
	-			invention (including antibodies	sclerosis and/or as described
				and agonists or antagonists of	below) and
		·		the invention) include assays	immunodeficiencies (e.g., as
				disclosed in Berger et al., Gene	described below). Additional
				66:1-10 (1988); Cullen and	highly preferred indications

	Malm. Methods in Enzymol	include inflammation and
	216:362-368 (1992): Henthorn	inflammatory disorders.
	et al., Proc Natl Acad Sci USA	Highly preferred indications
	85:6342-6346 (1988);	also include neoplastic
	Rellahan et al., J Biol Chem	diseases (e.g., leukemia,
	272(49):30806-30811 (1997);	lymphoma, and/or as described
	Chang et al., Mol Cell Biol	below under
	 18(9):4986-4993 (1998); and	"Hyperproliferative
	Fraser et al., Eur J Immunol	Disorders"). Highly preferred
	29(3):838-844 (1999), the	indications include neoplasms
	 contents of each of which are	and cancers, such as, leukemia,
	herein incorporated by	lymphoma, prostate, breast,
	 reference in its entirety.	lung, colon, pancreatic,
	 Human T cells that may be	esophageal, stomach, brain,
	 used according to these assays	liver, and urinary cancer. Other
	 are publicly available (e.g.,	preferred indications include
	through the ATCC).	benign dysproliferative
	 Exemplary human T cells that	disorders and pre-neoplastic
	 may be used according to these	conditions, such as, for
	assays include the SUPT cell	example, hyperplasia,
	 line, which is an IL-2 and IL-4	metaplasia, and/or dysplasia.
	 responsive suspension-culture	Preferred indications include
	 cell line.	arthritis, asthma, AIDS,
		allergy, anemia, pancytopenia,
_	 - 1	leukopenia, thrombocytopenia,
	 	Hodgkin's disease, acute
	 	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
-		granulomatous disease,
		inflammatory bowel disease,

Additional highly preferred indications include	inflammation and	inflammatory disorders.	Highly preferred indications	include autoimmune diseases	(e.g., rheumatoid arthritis,	systemic lupus erythematosis,	multiple sclerosis and/or as	described below),	immunodeficiencies (e.g., as	described below), boosting a T	cell-mediated immune	response, and suppressing a T	cell-mediated immune	response. Highly preferred	indications include neoplastic	diseases (e.g., melanoma, renal	cell carcinoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, for	example, melanoma (e.g.,	metastatic melanoma), renal	cell carcinoma (e.g., metastatic	renal cell carcinoma),	leukemia, lymphoma (e.g., T	cell lymphoma) and prostate
McGuire and Iacobelli, J Immunol 159(3):1319-1327	(1997); Parra et al., J Immunol	166(4):2437-2443 (2001); and	Butscher et al., J Biol Chem	3(1):552-560 (1998), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.												
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	becaute the colon manager
	oreast, mile, colon, panereant,
	esophageal, stomach, brain,
	liver and urinary cancer. Other
	preferred indications include
	benign dysproliferative
	disorders and pre-neoplastic
	conditions, such as, for
	example, hyperplasia,
	metaplasia, and/or dysplasia.
	A highly preferred indication
	includes infection (e.g.,
	AIDS, tuberculosis, infections
	associated with granulomatous
	disease, and osteoporosis,
	and/or as described below
	under "Infectious Disease"). A
	highly preferred indication is
	AIDS. Additional highly
	preferred indications include
	suppression of immune
-	reactions to transplanted
	organs and/or tissues, uveitis,
	psoriasis, and tropical spastic
	paraparesis. Preferred
	indications include blood
	disorders (e.g., as described
	below under "Immune
	Activity", "Blood-Related
	Disorders", and/or
 	"Cardiovascular Disorders").
	Preferred indications also

					include anemia, pancytopenia, leukopenia, thrombocytopenia, Hodgkin's disease, acute lymphocytic anemia (ALL), plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease,
317	HLWCF05	1265	Activation of transcription through NFAT response element in immune cells (such as T-cells).	Assays for the activation of transcription through the Nuclear Factor of Activated T cells (NFAT) response element are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate NFAT transcription factors and modulate expression of genes involved in immunomodulatory functions.	Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), boosting a T cell-mediated immune response, and suppressing a T

response. Additional highly preferred indications include inflammation and	additional highly preferred indication is infection (e.g., an	infectious disease as described below under "Infectious Disease"). Preferred	indications include neoplastic diseases (e.g., leukemia, lymphoma, and/or as described	below under "Hyperproliferative"	Disorders"). Preferred	and cancers, such as, for	example, leukemia, lymphoma, and prostate, breast, lung,	colon, pancreatic, esophageal, stomach, brain, liver and	urinary cancer. Other preferred	indications include benign dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	Preferred indications also	include anemia, pancytopenia,		Hodgkin's disease, acute
NFAT response element that may be used or routinely modified to test NFAT-	polypeptides of the invention (including antibodies and	invention) include assays disclosed in Berger et al., Gene	Malm, Methods in Enzymol 216:362-368 (1992): Henthorn	et al., Proc Natl Acad Sci USA 85:6342-6346 (1988): Serfling	et al., Biochim Biophys Acta	et al., Int J Biochem Cell Biol	31(10):1221-1236 (1999); Fraser et al., Eur J Immunol	29(3):838-844 (1999); and Yeseen et al., J Biol Chem	268(19):14285-14293 (1993),	the contents of each of which are herein incorporated by	reference in its entirety. T	cells that may be used	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these
							. <u>. </u>									

assays include the SUPT cell lymphocytic anemia (ALL), plasmacytomas, multiple culture of IL-2 and IL-4 arthritis, AIDS, granulomatous disease, inflammatory bowel disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, asthma and alleroy	Assays for the activation of transcription through the NFKB response element are well-known in the art and may be used or routinely modified to assess the ability of assess the ability of including antibodies and agonists or antagonists of the invention) to regulate NFKB Highly preferred indications include autoimmune diseases modulate expression of transcription factors and multiple sclerosis and/or as described below), and
	Activation of transcription through NFKB response element in immune cells (such as T-cells).
	1265
	HLWCF05
	317

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additional highly preferred	indication is infection (e.g.,	AIDS, and/or an infectious	disease as described below	under "Infectious Disease").	Highly preferred indications	include neoplastic diseases	(e.g., melanoma, leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such	as,melanoma, renal cell	carcinoma, leukemia,	lymphoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications also	include anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	l lymphocytic anemia (ALL).
modified to test NFKB-	response element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1998); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988); Black et	al., Virus Gnes 15(2):105-117	(1997); and Fraser et al.,	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety. T	cells that may be used	according to these assays are	publicly available (e.g.,	through the ATCC).	Exemplary human T cells that	may be used according to these	assays include the SUPT cell	line, which is a suspension	culture of IL-2 and IL-4	responsive T cells.			
			,																											

			-		plasmacytomas, multiple myeloma, Burkitt's lymphoma, arthritis, AIDS, granulomatous disease, inflammatory bowel disease, sepsis, neutropenia, neutrophilia, psoriasis, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, suppression of immune reactions to transplanted
318	HLYAC95	1266	Glucose Production in H4IIE		organic, admina and anorgy.
318	HLYAC95	1266	Production of IFNgamma using a T cells	IFNgamma FMAT. IFNg plays a central role in the immune system and is considered to be a proinflammatory cytokine. IFNg promotes TH1 and inhibits TH2 differentiation; promotes IgG2a and inhibits IgE secretion; induces macrophage activation; and increases MHC expression. Assays for immunomodulatory proteins produced by T cells and NK cells that regulate a variety of inflammatory activities and inhibit TH2 helper cell functions are well	A highly preferred embodiment of the invention includes a method for stimulating the production of IFNg. An alternative highly preferred embodiment of the invention includes a method for inhibiting the production of IFNg. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., viral

used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to mediate imhammatory activities, modulate TH2 helper cell function, and/or mediate humoral or cell-mediated immunity. Exemplary assays that test for immunomodulatory proteins evaluate the production of cytokines, such as Interferon gamma (IFNg), and the activation of T cells. Such assays that may be used or routinely modified to test immunomodulatory activity of polypeptides of the invention (including antibodies and		infections associated with chronic granulomatosus disease and malignant osteoporosis, and/or as described below under "Infectious Disease"). Highly preferred indications include autoimmune disease (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described below), immunodeficiency (e.g., as described below), boosting a T cell-mediated immune response, and
used or rounnery assess the ability polypeptides of th (including antibo agonists or antage invention) to mec immunomodulati inflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T cc assays that may t routinely modific immunomodulate polypeptides of t (including antibo)		ons associated with c granulomatosus e and malignant orosis, and/or as sed below under thous Disease"). Highly ed indications include mune disease (e.g., atoid arthritis, systemic srythematosis, multiple sis and/or as described bis and/or as described is described below), and a T cell-mediated he response, and
assess the ability polypeptides of th (including antibo agonists or antag invention) to mec immunomodulati inflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T cc assays that may b routinely modific immunomodulate polypeptides of t (including antibo)		c granulomatosus e and malignant orosis, and/or as bed below under tious Disease"). Highly ed indications include mune disease (e.g., atoid arthritis, systemic erythematosis, multiple sis and/or as described bis inmunodeficiency is described below), and a T cell-mediated he response, and
(including antibo agonists or antagonists or antagonismunomodulati inflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunomodulate evaluate the prodocytokines, such a gamma (IFNg), a activation of T or assays that may I routinely modific immunomodulate polypeptides of t (including antibo) (including antibo)		e and malignant orosis, and/or as bed below under tious Disease"). Highly ed indications include mune disease (e.g., atoid arthritis, systemic rrythematosis, multiple is and/or as described is immunodeficiency as described below), and a T cell-mediated he response, and
(including antibo agonists or antagonists or antagonists or antagonists or antagonism unannomodulati inflammatory act modulate TH2 he function, and/or 1 humoral or cell-nimmunity. Exemplate test for immunomodulate evaluate the prodocytokines, such a gamma (IFNg), a activation of T ce assays that may be routinely modific immunomodulate polypeptides of t (including antibo) (including antibo)		orosis, and/or as sed below under tious Disease"). Highly ed indications include imune disease (e.g., atoid arthritis, systemic erythematosis, multiple sis and/or as described, immunodeficiency is described below), ng a T cell-mediated ie response, and
agonists or antaginvention) to mecimmunomodulatinflammatory act modulate TH2 he function, and/or whumoral or cell-nimmunity. Exemple that test for immunomodulate evaluate the production of T ce assays that may be routinely modific immunomodulate polypeptides of t (including antibo).		bed below under tious Disease"). Highly ed indications include mune disease (e.g., atoid arthritis, systemic srythematosis, multiple is and/or as described; immunodeficiency is described below), and a T cell-mediated he response, and
invention) to mec immunomodulati inflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may be routinely modific immunomodulate polypeptides of to (including antibo).		tious Disease"). Highly red indications include mune disease (e.g., atoid arthritis, systemic rrythematosis, multiple is and/or as described; immunodeficiency is described below), ag a T cell-mediated he response, and
imflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may t routinely modifie immunomodulate polypeptides of t (including antibo		red indications include imune disease (e.g., atoid arthritis, systemic erythematosis, multiple sits and/or as described, immunodeficiency is described below), and a T cell-mediated ie response, and sssing a T cell-mediated
inflammatory act modulate TH2 he function, and/or 1 humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may b routinely modifie immunomodulate polypeptides of t (including antibo		mune disease (e.g., atoid arthritis, systemic rrythematosis, multiple sis and/or as described; immunodeficiency is described below), ag a T cell-mediated he response, and sssing a T cell-mediated
modulate TH2 he function, and/or r humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T c assays that may t routinely modific immunomodulate polypeptides of t (including antibo		atoid arthritis, systemic erythematosis, multiple sis and/or as described, immunodeficiency is described below), ag a T cell-mediated he response, and ssing a T cell-mediated essing a T cell-mediated
function, and/or I humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T or assays that may be routinely modific immunomodulate polypeptides of t (including antibo) (including antibo)		erythematosis, multiple sis and/or as described, immunodeficiency is described below), ng a T cell-mediated ie response, and ssing a T cell-mediated is ssing a T cell-mediated
humoral or cell-n immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may b routinely modific immunomodulate polypeptides of t (including antibo		is and/or as described, immunodeficiency is described below), ag a T cell-mediated ie response, and issing a T cell-mediated
immunity. Exem that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T c assays that may b routinely modific immunomodulate polypeptides of t (including antibo		is described below), as described below), as a T cell-mediated he response, and a T cell-mediated ssing a T cell-mediated
that test for immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T cc assays that may t routinely modific immunomodulate polypeptides of t (including antibo		is described below), ng a T cell-mediated ie response, and ssing a T cell-mediated
immunomodulate evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may b routinely modifie immunomodulate polypeptides of t (including antibo		ng a T cell-mediated ne response, and ssing a T cell-mediated
evaluate the prod cytokines, such a gamma (IFNg), a activation of T ce assays that may b routinely modific immunomodulate polypeptides of t (including antibo		ie response, and ssing a T cell-mediated
cytokines, such a gamma (IFNg), a activation of T ce assays that may be routinely modifice immunomodulate polypeptides of the continuous antibo (including antibo		ssing a T cell-mediated
gamma (IFNg), a activation of T ce assays that may be routinely modified immunomodulate polypeptides of the fincluding antibo		manufactor than a morning
activation of T ce assays that may be routinely modified immunomodulate polypeptides of the continuous antibotion including antibotion antibotion including antibotion antibotion and antibotion antibotio	_	immune response. Additional
assays that may b routinely modifie immunomodulate polypeptides of the fineluding antibo		highly preferred indications
routinely modifie immunomodulate polypeptides of tl (including antibo		include inflammation and
immunomodulate polypeptides of tl		inflammatory disorders.
polypeptides of the polype		Additional preferred
(including antibo		indications include idiopathic
		pulmonary fibrosis. Highly
agonists or antagonists of the		preferred indications include
invention) include the assays		neoplastic diseases (e.g.,
disclosed in Miraglia et al., J	_	leukemia, lymphoma,
Biomolecular Screening 4:193-	93-	melanoma, and/or as described
204 (1999); Rowland et al.,	wland et al., below under	under
"Lymphocytes: a practical		"Hyperproliferative
approach" Chapter 6:138-160	_	Disorders"). Highly preferred

indications include neoplasms and cancers, such as, for	example, leukemia, lymphoma, melanoma, and prostate,	breast, lung, colon, pancreatic,	esophageal, stomach, brain,	liver and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neoplastic	conditions, such as, for	example, hyperplasia,	metaplasia, and/or dysplasia.	Preferred indications include	anemia, pancytopenia,	leukopenia, thrombocytopenia,	Hodgkin's disease, acute	lymphocytic anemia (ALL),	plasmacytomas, multiple	myeloma, Burkitt's lymphoma,	arthritis, AIDS, granulomatous	disease, inflammatory bowel	disease, sepsis, neutropenia,	neutrophilia, psoriasis,	suppression of immune	reactions to transplanted	organs and tissues,	hemophilia, hypercoagulation,	diabetes mellitus, endocarditis,	meningitis, Lyme Disease,	acthmo and allarary
(2000); Gonzalez et al., J Clin Lab Anal 8(5):225-233 (1995);	Sci 856:22-32 (1998); Boehm	et al., Annu Rev Immunol	15:749-795 (1997), and	Rheumatology (Oxford)	38(3):214-20 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Human T cells that may be	used according to these assays	may be isolated using	techniques disclosed herein or	otherwise known in the art.	Human T cells are primary	human lymphocytes that	mature in the thymus and	express a T Cell receptor and	CD3, CD4, or CD8. These	cells mediate humoral or cell-	mediated immunity and may	be preactivated to enhance	responsiveness to	immunomodulatory factors.					
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	HLYAC95	1266	Stimulation of	Assays for measuring secretion	A highly preferred
318			insulin secretion	of insulin are well-known in	indication is diabetes mellitus.
			from pancreatic	the art and may be used or	An additional highly preferred
			beta cells.	routinely modified to assess	indication is a complication
				the ability of polypeptides of	associated with diabetes (e.g.,
				the invention (including	diabetic retinopathy, diabetic
				antibodies and agonists or	nephropathy, kidney disease
				antagonists of the invention) to	(e.g., renal failure,
				stimulate insulin secretion.	nephropathy and/or other
				For example, insulin secretion	diseases and disorders as
				is measured by FMAT using	described in the "Renal
				anti-rat insulin antibodies.	Disorders" section below),
				Insulin secretion from	diabetic neuropathy, nerve
				pancreatic beta cells is	disease and nerve damage
				upregulated by glucose and	(e.g., due to diabetic
				also by certain	neuropathy), blood vessel
				proteins/peptides, and	blockage, heart disease, stroke,
				disregulation is a key	impotence (e.g., due to diabetic
				component in diabetes.	neuropathy or blood vessel
				Exemplary assays that may be	blockage), seizures, mental
				used or routinely modified to	confusion, drowsiness,
				test for stimulation of insulin	nonketotic hyperglycemic-
				secretion (from pancreatic	hyperosmolar coma,
				cells) by polypeptides of the	cardiovascular disease (e.g.,
-				invention (including antibodies	heart disease, atherosclerosis,
				and agonists or antagonists of	microvascular disease,
				the invention) include assays	hypertension, stroke, and other
				disclosed in: Ahren, B., et al.,	diseases and disorders as
				Am J Physiol, 277(4 Pt	described in the
				2):R959-66 (1999); Li, M., et	"Cardiovascular Disorders"
				al., Endocrinology,	section below), dyslipidemia,

				138(9):3735-40 (1997): Kim	andooring disorders for
				12 (7) (1771), 1xmm,	
				N.H., et al., FEBS Lett,	described in the "Endocrine
				377(2):237-9 (1995); and,	Disorders" section below),
	100			Miraglia S et. al., Journal of	neuropathy, vision impairment
				Biomolecular Screening,	(e.g., diabetic retinopathy and
				4:193-204 (1999), the contents	blindness), ulcers and impaired
.				of each of which is herein	wound healing, and infection
				incorporated by reference in its	(e.g., infectious diseases and
				entirety. Pancreatic cells that	disorders as described in the
				may be used according to these	"Infectious Diseases" section
				assays are publicly available	below, especially of the
				(e.g., through the ATCC)	urinary tract and skin), carpal
				and/or may be routinely	tunnel syndrome and
				generated. Exemplary	Dupuytren's contracture).
	-			pancreatic cells that may be	An additional highly preferred
				used according to these assays	indication is obesity and/or
				include rat INS-1 cells. INS-1	complications associated with
				cells are a semi-adherent cell	obesity. Additional highly
				line established from cells	preferred indications include
				isolated from an X-ray induced	weight loss or alternatively,
				rat transplantable insulinoma.	weight gain. Aditional
				These cells retain	highly preferred indications are
				characteristics typical of native	complications associated with
				pancreatic beta cells including	insulin resistance.
				glucose inducible insulin	
				secretion. References: Asfari	
	_			et al. Endocrinology 1992	
				130:167.	
318	HLYAC95	1266	Hexosaminidase in		
	HI VAESO	1767	SEAD:		
	11111100	170/	SEAF III		

319			NK16/STAT6		
320	HLYAN59	1268	CD152 in Human T		
320	HLYAN59	1268	HLA-DR in Human T cells	,	
-	HLYAN59	1268	Production of	Assays for measuring	Highly preferred indications
320			VCAM in	expression of VCAM are well-	include inflammation (acute
			endothelial cells	known in the art and may be	and chronic), restnosis,
			(such as human	used or routinely modified to	atherosclerosis, asthma and
			umbilical vein	assess the ability of	allergy. Highly preferred
			endothelial cells	polypeptides of the invention	indications include
			(HUVEC))	(including antibodies and	inflammation and
				agonists or antagonists of the	inflammatory disorders,
				invention) to regulate VCAM	immunological disorders,
		-		expression. For example,	neoplastic disorders (e.g.
				FMAT may be used to meaure	cancer/tumorigenesis), and
		-		the upregulation of cell surface	cardiovascular disorders (such
				VCAM-1 expresssion in	as described below under
				endothelial cells. Endothelial	"Immune Activity", "Blood-
				cells are cells that line blood	Related Disorders",
				vessels, and are involved in	"Hyperproliferative Disorders"
		8		functions that include, but are	and/or "Cardiovascular
				not limited to, angiogenesis,	Disorders"). Highly preferred
				vascular permeability, vascular	indications include neoplasms
				tone, and immune cell	and cancers such as, for
				extravasation. Exemplary	example, leukemia, lymphoma,
				endothelial cells that may be	melanoma, renal cell
				used according to these assays	carcinoma, and prostate,
				include human umbilical vein	breast, lung, colon, pancreatic,
			-	endothelial cells (HUVEC),	esophageal, stomach, brain,
				which are available from	liver and urinary cancer. Other

preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia, and/or dysplasia.	A highly preferred embodiment of the invention includes a method for stimulating adipocyte proliferation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte proliferation. A highly preferred embodiment of the invention includes a method for stimulating adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. An alternative highly preferred embodiment of the invention includes a method for inhibiting adipocyte differentiation. A highly
commercial sources. The expression of VCAM (CD106), a membraneassociated protein, can be upregulated by cytokines or other factors, and contributes to the extravasation of lymphocytes, leucocytes and other immune cells from blood vessels; thus VCAM expression plays a role in promoting immune and inflammatory responses.	Kinase assay. Kinase assays, for example an Elk-1 kinase assay, for ERK signal transduction that regulate cell proliferation or differentiation are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to promote or inhibit cell proliferation, activation, and differentiation. Exemplary assays for ERK kinase activity that may be used or routinely modified to test ERK kinase-induced
	Activation of Adipocyte ERK Signaling Pathway
	1269
	HLYAP91
	321

	activity of polypeptides of the	preferred embodiment of the
	invention (including antibodies	invention includes a method
	and agonists or antagonists of	for stimulating (e.g.,
	the invention) include the	increasing) adipocyte
	assays disclosed in Forrer et	activation. An alternative
	al., Biol Chem 379(8-9):1101-	highly preferred embodiment
	1110 (1998); Le Marchand-	of the invention includes a
	Brustel Y, Exp Clin	method for inhibiting the
	Endocrinol Diabetes	activation of (e.g., decreasing)
	107(2):126-132 (1999);	and/or inactivating adipocytes.
	Kyriakis JM, Biochem Soc	Highly preferred indications
	Symp 64:29-48 (1999); Chang	include endocrine disorders
	and Karin, Nature	(e.g., as described below under
`	410(6824):37-40 (2001); and	"Endocrine Disorders").
	Cobb MH, Prog Biophys Mol	Highly preferred indications
	Biol 71(3-4):479-500 (1999);	also include neoplastic
	the contents of each of which	diseases (e.g., lipomas,
	are herein incorporated by	liposarcomas, and/or as
	reference in its entirety.	described below under
	Mouse adipocyte cells that	"Hyperproliferative
	may be used according to these	Disorders"). Preferred
	assays are publicly available	indications include blood
	(e.g., through the ATCC).	disorders (e.g., hypertension,
	Exemplary mouse adipocyte	congestive heart failure, blood
	cells that may be used	vessel blockage, heart disease,
	according to these assays	stroke, impotence and/or as
<u> </u>	include 3T3-L1 cells. 3T3-L1	described below under
	is an adherent mouse	"Immune Activity",
	preadipocyte cell line that is a	"Cardiovascular Disorders",
	continuous substrain of 3T3	and/or "Blood-Related
	fibroblast cells developed	Disorders"), immune disorders

through	through clonal isolation and	(e.g., as described below under
adip	adipose-like conversion under	disorders (e.g., as described
appr	appropriate differentiation	below under "Neural Activity
cond	conditions known in the art.	and Neurological Diseases"),
		and infection (e.g., as
		described below under
		"Infectious Disease").
		A highly preferred indication
		is diabetes mellitus. An
		additional highly preferred
		indication is a complication
	J	associated with diabetes (e.g.,
	•	diabetic retinopathy, diabetic
		nephropathy, kidney disease
		(e.g., renal failure,
		nephropathy and/or other
		diseases and disorders as
-		described in the "Renal
		Disorders" section below),
		diabetic neuropathy, nerve
		disease and nerve damage
		(e.g., due to diabetic
		neuropathy), blood vessel
		blockage, heart disease, stroke,
		impotence (e.g., due to diabetic
		neuropathy or blood vessel
		blockage), seizures, mental
		confusion, drowsiness,
		nonketotic hyperglycemic-
		hyperosmolar coma,

cardiovascular disease (e.g.,	neart disease, atheroscierosis, microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below (particularly of the	urinary tract and skin). An	additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	complications associated with	insulin resistance.	Additional highly preferred
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indications are disorders of the
musculoskeletal systems
including myopathies,
muscular dystrophy, and/or as
described herein,
Additional highly preferred
indications include,
hypertension, coronary artery
disease, dyslipidemia,
gallstones, osteoarthritis,
degenerative arthritis, eating
disorders, fibrosis, cachexia,
and kidney diseases or
 disorders. Preferred
indications include neoplasms
and cancer, such as,
i lymphoma, leukemia and
breast, colon, and kidney
cancer. Additional preferred
indications include melanoma,
prostate, lung, pancreatic,
esophageal, stomach, brain,
liver, and urinary cancer.
 Highly preferred indications
include lipomas and
liposarcomas. Other preferred
indications include benign
dysproliferative disorders and
pre-neoplastic conditions, such
as, for example, hyperplasia,
metaplasia, and/or dysplasia.

	HLYAZ61	1270	Activation of JNK	Kinase assav. JNK kinase	Highly preferred indications
322			Signaling Pathway	assays for signal transduction	include asthma, allergy,
			in immune cells	that regulate cell proliferation,	hypersensitivity reactions,
			(such as	activation, or apoptosis are	inflammation, and
-			eosinophils).	well known in the art and may	inflammatory disorders.
				be used or routinely modified	Additional highly preferred
				to assess the ability of	indications include immune
				polypeptides of the invention	and hematopoietic disorders
				(including antibodies and	(e.g., as described below under
				agonists or antagonists of the	"Immune Activity", and
			~~	invention) to promote or	"Blood-Related Disorders"),
				inhibit cell proliferation,	autoimmune diseases (e.g.,
				activation, and apoptosis.	rheumatoid arthritis, systemic
				Exemplary assays for JNK	lupus erythematosis, Crohn"s
				kinase activity that may be	disease, multiple sclerosis
				used or routinely modified to	and/or as described below),
				test JNK kinase-induced	immunodeficiencies (e.g., as
				activity of polypeptides of the	described below). Highly
				invention (including antibodies	preferred indications also
				and agonists or antagonists of	include boosting or inhibiting
				the invention) include the	immune cell proliferation.
				assays disclosed in Forrer et	Preferred indications include
				al., Biol Chem 379(8-9):1101-	neoplastic diseases (e.g.,
				1110 (1998); Gupta et al., Exp	leukemia, lymphoma, and/or as
				Cell Res 247(2): 495-504	described below under
				(1999); Kyriakis JM, Biochem	"Hyperproliferative
				Soc Symp 64:29-48 (1999);	Disorders"). Highly preferred
				Chang and Karin, Nature	indications include boosting an
				410(6824):37-40 (2001); and	eosinophil-mediated immune
				Cobb MH, Prog Biophys Mol	response, and suppressing an
				Biol 71(3-4):479-500 (1999);	eosinophil-mediated immune

response.																														The second secon
the contents of each of which	are herein incorporated by	reference in its entirety.	Exemplary cells that may be	used according to these assays	include eosinophils.	Eosinophils are important in	the late stage of allergic	reactions; they are recruited to	tissues and mediate the	inflammatory response of late	stage allergic reaction.	Moreover, exemplary assays	that may be used or routinely	modified to assess the ability	of polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) to modulate	signal transduction, cell	proliferation, activation, or	apoptosis in eosinophils	include assays disclosed and/or	cited in: Zhang JP, et al., "Role	of caspases in dexamethasone-	induced apoptosis and	activation of c-Jun NH2-	terminal kinase and p38	mitogen-activated protein	kinase in human eosinophils"	Clin Exp Immunol;
			-						1																	-				
	-																-													

																						Preferred indications	include neoplastic diseases	(e.g., as described below under	"Hyperproliferative	Disorders"), blood disorders	(e.g., as described below under	"Immune Activity",	"Cardiovascular Disorders",	and/or "Blood-Related
Oct;122(1):20-7 (2000);	Hebestreit H, et al.,	"Disruption of fas receptor	signaling by nitric oxide in	eosinophils" J Exp Med; Feb	2;187(3):415-25 (1998); J	Allergy Clin Immunol 1999	Sep;104(3 Pt 1):565-74; and,	Sousa AR, et al., "In vivo	resistance to corticosteroids in	bronchial asthma is associated	with enhanced	phosyphorylation of JUN N-	terminal kinase and failure of	prednisolone to inhibit JUN N-	terminal kinase	phosphorylation" J Allergy	Clin Immunol; Sep;104(3 Pt	1):565-74 (1999); the contents	of each of which are herein	incorporated by reference in its	entirety.	Assays for the activation of	transcription through the AP1	response element are known in	the art and may be used or	routinely modified to assess	the ability of polypeptides of	-	antibodies and agonists or	n) to
																						Activation of	transcription	through AP1	response element in	immune cells (such	as T-cells).			
		-1-																				1271								
																						HLYBD32								
																						(323							

																												_		
Disorders"), and infection	(e.g., an infectious disease as	described below under	"Infectious Disease"). Highly	preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	highly preferred indications	include inflammation and	inflammatory disorders.	Highly preferred indications	also include neoplastic	diseases (e.g., leukemia,	lymphoma, and/or as described	below under	"Hyperproliferative	Disorders"). Highly preferred	indications include neoplasms	and cancers, such as, leukemia,	lymphoma, prostate, breast,	lung, colon, pancreatic,	esophageal, stomach, brain,	liver, and urinary cancer. Other	preferred indications include	benign dysproliferative	disorders and pre-neonlastic
modulate growth and other cell	functions. Exemplary assays	for transcription through the	AP1 response element that	may be used or routinely	modified to test AP1-response	element activity of	polypeptides of the invention	(including antibodies and	agonists or antagonists of the	invention) include assays	disclosed in Berger et al., Gene	66:1-10 (1988); Cullen and	Malm, Methods in Enzymol	216:362-368 (1992); Henthorn	et al., Proc Natl Acad Sci USA	85:6342-6346 (1988);	Rellahan et al., J Biol Chem	272(49):30806-30811 (1997);	Chang et al., Mol Cell Biol	18(9):4986-4993 (1998); and	Fraser et al., Eur J Immunol	29(3):838-844 (1999), the	contents of each of which are	herein incorporated by	reference in its entirety.	Mouse T cells that may be	used according to these assays	are publicly available (e.g.,	through the ATCC).	Exemplary manice T cells that
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						-						,																		

				may be used according to these assays include the HT2 cell	conditions, such as, for example hypermlasia
•				line, which is an IL-2	metaplasia, and/or dysplasia.
•				dependent suspension culture	Preferred indications include
				cell line that also responds to	arthritis, asthma, AIDS,
				IL-4.	allergy, anemia, pancytopenia,
					leukopenia, thrombocytopenia,
					Hodgkin's disease, acute
					lymphocytic anemia (ALL),
-					plasmacytomas, multiple
					myeloma, Burkitt's lymphoma,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, psoriasis, suppression
					of immune reactions to
					transplanted organs and
					tissues, endocarditis,
					meningitis, and Lyme Disease.
	HLYES38	1272	Activation of	Kinase assay. Kinase assays,	A highly preferred
324			Adipocyte PI3	for example an GSK-3 assays,	embodiment of the invention
			Kinase Signalling	for PI3 kinase signal	includes a method for
			Pathway	transduction that regulate	increasing adipocyte survival
				glucose metabolism and cell	An alternative highly preferred
	,			survival are well-known in the	embodiment of the invention
				art and may be used or	includes a method for
, , , , , , , , , , , , , , , , , , ,				routinely modified to assess	decreasing adipocyte survival.
				the ability of polypeptides of	A preferred embodiment of the
				the invention (including	invention includes a method
				antibodies and agonists or	for stimulating adipocyte
				antagonists of the invention) to	proliferation. An alternative
				promote or inhibit glucose	highly preferred embodiment

	metabolism and cell survival.	of the invention includes a
	Exemplary assays for PI3	method for inhibiting
	kinase activity that may be	adipocyte proliferation. A
	used or routinely modified to	preferred embodiment of the
	test PI3 kinase-induced activity	invention includes a method
	of polypeptides of the	for stimulating adipocyte
	invention (including antibodies	differentiation. An alternative
	and agonists or antagonists of	highly preferred embodiment
	the invention) include assays	of the invention includes a
	disclosed in Forrer et al., Biol	method for inhibiting
	Chem 379(8-9):1101-1110	adipocyte differentiation.
	(1998); Nikoulina et al.,	Highly preferred indications
	Diabetes 49(2):263-271	include endocrine disorders
	(2000); and Schreyer et al.,	(e.g., as described below under
	Diabetes 48(8):1662-1666	"Endocrine Disorders").
	(1999), the contents of each of	Preferred indications include
	which are herein incorporated	neoplastic diseases (e.g.,
	by reference in its entirety.	lipomas, liposarcomas, and/or
	Mouse adipocyte cells that	as described below under
	may be used according to these	"Hyperproliferative
	assays are publicly available	Disorders"), blood disorders
	(e.g., through the ATCC).	(e.g., hypertension, congestive
	Exemplary mouse adipocyte	heart failure, blood vessel
	cells that may be used	blockage, heart disease, stroke,
	according to these assays	impotence and/or as described
	include 3T3-L1 cells. 3T3-L1	below under "Immune
	is an adherent mouse	Activity", "Cardiovascular
	preadipocyte cell line that is a	Disorders", and/or "Blood-
~	continous substrain of 3T3	Related Disorders"), immune
	fibroblast cells developed	disorders (e.g., as described
	through clonal isolation and	below under "Immune

		undergo a pre-adipocyte to	Activity"), neural disorders
		adipose-like conversion under	(e.g., as described below under
		appropriate differentiation	"Neural Activity and
		conditions known in the art.	Neurological Diseases"), and
			infection (e.g., as described
			below under "Infectious
			Disease"). A highly
			preferred indication is diabetes
			mellitus. An additional
			highly preferred indication is a
-			complication associated with
			diabetes (e.g., diabetic
			retinopathy, diabetic
			nephropathy, kidney disease
,			(e.g., renal failure,
	-		nephropathy and/or other
	-		diseases and disorders as
			described in the "Renal
	-		Disorders" section below),
			diabetic neuropathy, nerve
			disease and nerve damage (e.g,
	-		due to diabetic neuropathy),
			blood vessel blockage, heart
			disease, stroke, impotence
			(e.g., due to diabetic
			neuropathy or blood vessel
			blockage), seizures, mental
			confusion, drowsiness,
			nonketotic hyperglycemic-
			hyperosmolar coma,
			cardiovascular disease (e.g.,

heart disease, atherosclerosis.	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carpal	tunnel syndrome and	Dupuytren's contracture).	An additional highly preferred	indication is obesity and/or	complications associated with	obesity. Additional highly	preferred indications include	weight loss or alternatively,	weight gain. Additional	highly preferred indications are	
																	-												

Additional highly preferred indications are disorders of the	musculoskeletal systems	including myopathies,	muscular dystrophy, and/or as	described herein.	Additional highly preferred	indications include,	hypertension, coronary artery	disease, dyslipidemia,	gallstones, osteoarthritis,	degenerative arthritis, eating	disorders, fibrosis, cachexia,	and kidney diseases or	disorders. Highly preferred	indications include neoplasms	and cancer, such as, lipoma,	liposarcoma, lymphoma,	leukemia and breast, colon,	and kidney cancer. Additional	highly preferred indications	include melanoma, prostate,	lung, pancreatic, esophageal,	stomach, brain, liver, and	urinary cancer. Other preferred	indications include benign	dysproliferative disorders and	pre-neoplastic conditions, such	as, for example, hyperplasia,	metaplasia, and/or dysplasia.	
																													IFNg in Human T-
					343										,					-									1272
						-																							HLYES38

324			cell 2B9		
324	HLYES38	1272	TNFa in Human T-cell 2B9		
	HMADS41	1273	Protection from	Caspase Apoptosis Rescue.	A highly preferred
325			Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
			Apoptosis.	rescue are well known in the	includes a method for
				art and may be used or	stimulating endothelial cell
				routinely modified to assess	growth. An alternative highly
				the ability of the polypeptides	preferred embodiment of the
••				of the invention (including	invention includes a method
				antibodies and agonists or	for inhibiting endothelial cell
				antagonists of the invention) to	growth. A highly preferred
				inhibit caspase protease-	embodiment of the invention
				mediated apoptosis.	includes a method for
				Exemplary assays for caspase	stimulating endothelial cell
				apoptosis that may be used or	proliferation. An alternative
******				routinely modified to test	highly preferred embodiment
				caspase apoptosis rescue of	of the invention includes a
				polypeptides of the invention	method for inhibiting
				(including antibodies and	endothelial cell proliferation.
		,		agonists or antagonists of the	A highly preferred
				invention) include the assays	embodiment of the invention
<u>, </u>				disclosed in Romeo et al.,	includes a method for
· ·				Cardiovasc Res 45(3): 788-794	stimulating endothelial cell
				(2000); Messmer et al., Br J	growth. An alternative highly
			-	Pharmacol 127(7): 1633-1640	preferred embodiment of the
				(1999); and J Atheroscler	invention includes a method
	-			Thromb 3(2): 75-80 (1996);	for inhibiting endothelial cell
				the contents of each of which	growth. A highly preferred
				are herein incorporated by	embodiment of the invention
				reference in its entirety.	includes a method for

stimulating apoptosis of endothelial cells. An alternative highly preferred embodiment of the invention	includes a method for inhibiting (e.g., decreasing) apoptosis of endothelial cells. A highly preferred embodiment of the invention	includes a method for stimulating angiogenisis. An alternative highly preferred embodiment of the invention	includes a method for inhibiting angiogenesis. A highly preferred embodiment of the invention includes a	method for reducing cardiac hypertrophy. An alternative highly preferred embodiment of the invention includes a method for inducing cardiac hypertrophy. Highly	
Endothelial cells that may be used according to these assays are publicly available (e.g., through commercial sources).	Exemplary endothelial cells that may be used according to these assays include bovine aortic endothelial cells (bAEC), which are an example	of endothelial cells which line blood vessels and are involved in functions that include, but are not limited to,	angiogenesis, vascular permeability, vascular tone, and immune cell extravasation.		
					

		leukemias, and Kaposi"s sarcoma, and retinal disorders.
		Highly preferred indications
		include neoplasms and cancer,
		such as, Kaposi"s sarcoma, hemangioma (capillary and
		cavernous), glomus tumors,
		telangiectasia, bacillary
		angiomatosis,
		hemangioendothelioma,
		angiosarcoma,
		haemangiopericytoma,
		lymphangioma,
		lymphangiosarcoma. Highly
		preferred indications also
		include cancers such as,
		prostate, breast, lung, colon,
		pancreatic, esophageal,
		stomach, brain, liver, and
		urinary cancer. Preferred
		indications include benign
		dysproliferative disorders and
***************************************		pre-neoplastic conditions, such
		as, for example, hyperplasia,
		metaplasia, and/or dysplasia.
		Highly preferred indications
		also include arterial disease,
		such as, atherosclerosis,
		hypertension, coronary artery
		disease, inflammatory
		vasculitides. Revnaud"s

			disease and Reynaud"s
			phenomenom, aneurysms,
			restenosis; venous and
			lymphatic disorders such as
			thrombophlebitis,
			lymphangitis, and
			lymphedema; and other
			vascular disorders such as
			 peripheral vascular disease,
			and cancer. Highly
			preferred indications also
-			include trauma such as
			wounds, burns, and injured
			tissue (e.g., vascular injury
			such as, injury resulting from
			balloon angioplasty, and
			atheroschlerotic lesions),
		-	implant fixation, scarring,
			ischemia reperfusion injury,
			rheumatoid arthritis,
		-	cerebrovascular disease, renal
			diseases such as acute renal
			failure, and osteoporosis.
			 Additional highly preferred
	- 44.40		indications include stroke,
			graft rejection, diabetic or
			 other retinopathies, thrombotic
			and coagulative disorders,
			 vascularitis, lymph
			 angiogenesis, sexual disorders,
		and the second s	age-related macular

degeneration, and treatment /prevention of endometriosis and related conditions.	Additional highly preferred indications include fibromas,	heart disease, cardiac arrest,	vascular disease. Preferred	indications include blood	disorders (e.g., as described	below under "Immune Activity", "Blood-Related	Disorders", and/or	"Cardiovascular Disorders").	Preferred indications include	autoimmune diseases (e.g.,	rheumatoid arthritis, systemic	lupus erythematosis, multiple	sclerosis and/or as described	below) and	immunodeficiencies (e.g., as	described below). Additional	preferred indications include	inflammation and	inflammatory disorders (such	as acute and chronic	inflammatory diseases, e.g.,	inflammatory bowel disease	and Crohn's disease), and pain	management.	A highly preferred
																									Kinase assay. Kinase assays,
																			-						Activation of
														. 11-0-0-											1273
																									HMADS41

325	Henatocyte FRK	for example an FIL-1 Linase	embodiment of the invention
	inspance in the si	ocalinate an English to the	
	Signaling Pathway	assay, tor EKK signal	includes a method for
		transduction that regulate cell	stimulating hepatocyte cell
		proliferation or differentiation	proliferation. An alternative
		are well known in the art and	highly preferred embodiment
		may be used or routinely	of the invention includes a
		modified to assess the ability	method for inhibiting
		of polypeptides of the	hepatocyte cell proliferation.
		invention (including antibodies	A highly preferred
		and agonists or antagonists of	embodiment of the invention
	 	the invention) to promote or	includes a method for
		inhibit cell proliferation,	stimulating hepatocyte cell
	 	activation, and differentiation.	differentiation. An alternative
		Exemplary assays for ERK	highly preferred embodiment
		kinase activity that may be	of the invention includes a
109		used or routinely modified to	method for inhibiting
		test ERK kinase-induced	hepatocyte cell differentiation.
		activity of polypeptides of the	A highly preferred
		invention (including antibodies	embodiment of the invention
		and agonists or antagonists of	includes a method for
		the invention) include the	activating hepatocyte cells. An
		assays disclosed in Forrer et	alternative highly preferred
		al., Biol Chem 379(8-9):1101-	embodiment of the invention
		1110 (1998); Kyriakis JM,	includes a method for
		Biochem Soc Symp 64:29-48	inhibiting the activation of
		(1999); Chang and Karin,	and/or inactivating hepatocyte
		Nature 410(6824):37-40	cells. Highly preferred
	~~~	(2001); and Cobb MH, Prog	indications include disorders of
		Biophys Mol Biol 71(3-4):479-	the liver and/or endocrine
		500 (1999); the contents of	disorders (e.g., as described
		each of which are herein	below under "Endocrine

Disorders"). Preferred indications include neoplastic diseases (e.g., as described below under "Hyperproliferative Disorders"), blood disorders	(e.g., as described below under "Immune Activity", "Cardiovascular Disorders", and/or "Blood-Related Disorders"), immune disorders (e.g., as described below under	"Immune Activity"), neural disorders (e.g., as described below under "Neural Activity and Neurological Diseases"),	and infection (e.g., as described below under "Infectious Disease"). A highly preferred indication is diabetes mellitus. An	additional highly preferred indication is a complication associated with diabetes (e.g., diabetic retinopathy, diabetic nephronathy kidney disease	(e.g., renal failure, nephropathy and/or other diseases and disorders as described in the "Renal".  Disorders" section below),
incorporated by reference in its entirety. Rat liver hepatoma cells that may be used according to these assays are publicly available (e.g., through the ATCC).	Exemplary rat liver hepatoma cells that may be used according to these assays include H4lle cells, which are known to respond to glucocorticoids, insulin, or	cAMP derivatives.			

diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic	neuropathy), blood vessel	blockage, heart disease, stroke,	impotence (e.g., due to diabetic	neuropathy or blood vessel	blockage), seizures, mental	confusion, drowsiness,	nonketotic hyperglycemic-	hyperosmolar coma,	cardiovascular disease (e.g.,	heart disease, atherosclerosis,	microvascular disease,	hypertension, stroke, and other	diseases and disorders as	described in the	"Cardiovascular Disorders"	section below), dyslipidemia,	endocrine disorders (as	described in the "Endocrine	Disorders" section below),	neuropathy, vision impairment	(e.g., diabetic retinopathy and	blindness), ulcers and impaired	wound healing, infection (e.g.,	infectious diseases and	disorders as described in the	"Infectious Diseases" section	below, especially of the	urinary tract and skin), carnal
						-																							

tunnel syndrome and Dupuytren's contracture). An additional highly preferred indication is obesity and/or complications associated with	obesity. Additional highly preferred indications include weight loss or alternatively, weight gain. Additional highly preferred indications are complications associated with insulin resistance.	Additonal highly preferred indications are disorders of the musculoskeletal systems including myopathies, muscular dystrophy, and/or as described herein.  Additional highly preferred indications include, hepatitis, jaundice, gallstones, cirrhosis of the liver, degenerative or	necrotic liver disease, alcoholic liver diseases, fibrosis, liver regeneration, metabolic disease, dyslipidemia and chlolesterol metabolism. Additional highly preferred indications include neoplasms and cancers, such as

					hepatocarcinomas, other liver cancers, and colon and pancreatic cancer. Preferred indications also include prostate, breast, lung, esophageal, stomach, brain, and urinary cancer. Other preferred indications include benign dysproliferative disorders and pre-neoplastic conditions, such as, for example, hyperplasia, metaplasia and/or dysplasia
325	HMADS41	1273	Regulation of apoptosis of immune cells (such as mast cells).	Caspase Apoptosis. Assays for caspase apoptosis are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to regulate caspase protease-mediated apoptosis in immune cells (such as, for example, in mast cells). Mast cells are found in connective and mucosal tissues throughout the body, and their activation via immunoglobulin E - antigen, promoted by T helper cell type 2 cytokines, is an	Preferred embodiments of the invention include using polypeptides of the invention (or antibodies, agonists, or antagonists thereof) in detection, diagnosis, prevention, and/or treatment of asthma, allergy, hypersensitivity and inflammation.

	ation		Se	al.	ase	or			f the	odies	jo;		a A,		1);	Exp		ıt	Nor	-6	þ	mb		are			pesn	re		ss).
important component of	allergic disease. Dysregulation	of mast cell apoptosis may	play a role in allergic disease	and mast cell tumor survival.	Exemplary assays for caspase	apoptosis that may be used or	routinely modified to test	capase apoptosis activity	induced by polypeptides of the	invention (including antibodies	and agonists or antagonists of	the invention) include the	assays disclosed in: Masuda A,	et al., J Biol Chem,	276(28):26107-26113 (2001);	Yeatman CF 2nd, et al., J Exp	Med, 192(8):1093-1103	(2000);Lee et al., FEBS Lett	485(2-3): 122-126 (2000); Nor	et al., J Vasc Res 37(3): 209-	218 (2000); and Karsan and	Harlan, J Atheroscler Thromb	(3(2): 75-80 (1996); the	contents of each of which are	herein incorporated by	reference in its entirety.	Immune cells that may be used	according to these assays are	publicly available (e.g.,	through commercial sources).
	-													-																
																± 14														

me cells that ording to these ast cells such an mast cell	s strong embodiment of the invention includes a method for stimulating (e.g., increasing) and increases lightly preferred embodiment of the invention includes a highly preferred embodiment of the invention includes a method for inhibiting (e.g., ession of IL-6 production. A pautoimmune highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Bloodhere the strongly and infection (e.g., as described below under "Cardiovascular Disorders"), and infections Disease"). Highly modified to autoimmune diseases (e.g., rhe invention includes and infection diseases (e.g., as autoimmune diseases (e.g., as autoimmune diseases (e.g., and infections Diseases). Highly preferred indications include autoimmune diseases (e.g., and infection diseases (e.g., and infection diseases). Highly preferred indications include autoimmune diseases (e.g., and infection diseases). Highly preferred indications include autoimmune diseases (e.g., and infection diseases). Highly preferred indications include autoimmune diseases (e.g., as autoimmune diseases (e.g., as autoimmune diseases (e.g., as autoimmune diseases), Highly preferred indications include autoimmune diseases (e.g., as autoimmune diseases), Highly preferred indications include autoimmune diseases (e.g., as autoimmune diseases), Highly preferred indications include autoimmune diseases (e.g., as autoimmune diseases (e.g., autoimmune diseases (e.g., autoimmune diseases (e.g., autoimmune diseases (e.g., autoimmune diseases	1
Exemplary immune cells that may be used according to these assays include mast cells such as the HMC human mast cell line.	Production of IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and	odt to stainonatus ac stainona
	73 1274	
	326 HMADU73	

	invention) to mediate	below) and
	immunomodulation and	immunodeficiencies (e.g., as
	differentiation and modulate T	described below). Highly
	cell proliferation and function.	preferred indications also
	Exemplary assays that test for	include boosting a B cell-
	immunomodulatory proteins	mediated immune response
	 evaluate the production of	and alternatively suppressing a
	 cytokines, such as IL-6, and	B cell-mediated immune
	the stimulation and	response. Highly preferred
	upregulation of T cell	indications include
	proliferation and functional	inflammation and
	activities. Such assays that	inflammatory
	may be used or routinely	disorders.Additional highly
	modified to test	preferred indications include
	immunomodulatory and	asthma and allergy. Highly
	diffferentiation activity of	preferred indications include
	polypeptides of the invention	neoplastic diseases (e.g.,
	(including antibodies and	myeloma, plasmacytoma,
	agonists or antagonists of the	leukemia, lymphoma,
	invention) include assays	melanoma, and/or as described
	disclosed in Miraglia et al., J	below under
	Biomolecular Screening 4:193-	"Hyperproliferative
	204(1999); Rowland et al.,	Disorders"). Highly preferred
	"Lymphocytes: a practical	indications include neoplasms
	approach" Chapter 6:138-160	and cancers, such as, myeloma,
	(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
	Immunol 158:2919-2925	lymphoma, melanoma, and
•	(1997), the contents of each of	prostate, breast, lung, colon,
	which are herein incorporated	pancreatic, esophageal,
	by reference in its entirety.	stomach, brain, liver and
	Human dendritic cells that may   urinary cancer. Other preferred	urinary cancer. Other preferred

				be used according to these	indications include benign
				assays may be isolated using	dysproliferative disorders and
				techniques disclosed herein or	pre-neoplastic conditions, such
				otherwise known in the art.	as, for example, hyperplasia,
				Human dendritic cells are	metaplasia, and/or dysplasia.
				antigen presenting cells in	Preferred indications include
				suspension culture, which,	anemia, pancytopenia,
				when activated by antigen	leukopenia, thrombocytopenia,
				and/or cytokines, initiate and	Hodgkin's disease, acute
				upregulate T cell proliferation	lymphocytic anemia (ALL),
				and functional activities.	multiple myeloma, Burkitt's
					lymphoma, arthritis, AIDS,
					granulomatous disease,
					inflammatory bowel disease,
					sepsis, neutropenia,
					neutrophilia, psoriasis,
					suppression of immune
					reactions to transplanted
					organs and tissues,
					hemophilia, hypercoagulation,
					diabetes mellitus, endocarditis,
					meningitis, and Lyme Disease.
					An additonal preferred
					indication is infection (e.g., an
					infectious disease as described
					below under "Infectious
					Disease").
	HMADU73	1274	Production of TNF	TNFa FMAT. Assays for	A highly preferred
326			alpha by dendritic	immunomodulatory proteins	embodiment of the invention
			cells	produced by activated	includes a method for
				macrophages, T cells,	inhibiting (e.g., decreasing)

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001/702	204(1999). Rowland et al	Highly preferred indications
		inging presence marcanons
dm/tr.		include neoplastic diseases
approac	approach" Chapter 6:138-160	(e.g., leukemia, lymphoma,
(2000);	(2000); Verhasselt et al., Eur J	and/or as described below
	Immunol 28(11):3886-3890	under "Hyperproliferative
(1198);	(1198); Dahlen et al., J	Disorders"). Additionally,
Immun	Immunol 160(7):3585-3593	highly preferred indications
(1998);	(1998); Verhasselt et al., J	include neoplasms and
Immun	Immunol 158:2919-2925	cancers, such as, leukemia,
(1997);	(1997); and Nardelli et al., J	lymphoma, melanoma, glioma
Leukoc	Leukoc Biol 65:822-828	(e.g., malignant glioma), solid
(1999),	(1999), the contents of each of	tumors, and prostate, breast,
which a	which are herein incorporated	lung, colon, pancreatic,
by refer	by reference in its entirety.	esophageal, stomach, brain,
Human	Human dendritic cells that may	liver and urinary cancer. Other
pe nsed	be used according to these	preferred indications include
assays I	assays may be isolated using	benign dysproliferative
techniq	techniques disclosed herein or	disorders and pre-neoplastic
otherwi	otherwise known in the art.	conditions, such as, for
Human	Human dendritic cells are	example, hyperplasia,
antigen		metaplasia, and/or dysplasia.
susbens		Preferred indications include
when ac	when activated by antigen	anemia, pancytopenia,
and/or c	and/or cytokines, initiate and	leukopenia, thrombocytopenia,
nbregul	upregulate T cell proliferation	Hodgkin's disease, acute
and fun	and functional activities.	lymphocytic anemia (ALL),
		plasmacytomas, multiple
		myeloma, Burkitt's lymphoma,
		arthritis, AIDS, granulomatous
		disease, inflammatory bowel
		disease, neutropenia,

neutrophilia, psoriasis, suppression of immune reactions to transplanted organs and tissues, hemophilia, hypercoagulation, diabetes mellitus, endocarditis, meningitis, Lyme Disease, cardiac reperfusion injury, and asthma and allergy. An additional preferred indication is infection (e.g., an infectious disease as described below under "Infectious Disease").			on of IL-10 Highly preferred indications include allergy and asthma. Additional highly preferred modified indications include immune and hematopoietic disorders nath hematopoietic disorders (e.g., as described below under "Immune Activity", and "Blood-Related Disorders"), ate or autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, Crohn"s at may be disease, multiple sclerosis and/or as described below),
			Assays for production of IL-10 and activation of T-cells are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the invention) to stimulate or inhibit production of IL-10 and/or activation of T-cells. Exemplary assays that may be used or routinely modified to
	IgG in Human B cells SAC	CD152 in Human T cells	Production of IL-10 and activation of T-cells.
	1274	1274	1274
	HMADU73	HMADU73	HMADU73
	326	326	326

	polypeptides and antibodies of	described below), boosting a T
	the invention (including	cell-mediated immune
	agonists or antagonists of the	response, and suppressing a T
	invention) to modulate IL-10	cell-mediated immune
	production and/or T-cell	response.
	proliferation include, for	1
	example, assays such as	
-	disclosed and/or cited in:	
	Robinson, DS, et al., "Th-2	
	cytokines in allergic disease"	
	Br Med Bull; 56 (4): 956-968	
	(2000), and Cohn, et al., "T-	•
	helper type 2 cell-directed	
	therapy for asthma"	
	Pharmacology & Therapeutics;	
	88: 187-196 (2000); the	
	contents of each of which are	
	herein incorporated by	
	reference in their entirety.	
	Exemplary cells that may be	
	used according to these assays	
	include Th2 cells. IL10	
	secreted from Th2 cells may be	
	measured as a marker of Th2	
	cell activation. Th2 cells are	
	a class of T cells that secrete	
	IL4, IL10, IL13, IL5 and IL6.	
	Factors that induce	
	differentiation and activation	
	of Th2 cells play a major role	
	in the initiation and	

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	A highly preferred indication is diabetes mellitus. An additional highly preferred indication is a complication associated with diabetes (e.g.,	nephropathy, kidney disease (e.g., renal failure, nephropathy and/or other	diseases and disorders as described in the "Renal Disorders" section below), diabetic neuropathy, nerve disease and nerve damage	(e.g., due to diabetic neuropathy), blood vessel blockage, heart disease, stroke, impotence (e.g., due to diabetic	neuropathy or blood vessel blockage), seizures, mental confusion, drowsiness,	hyperosmolar coma, cardiovascular disease (e.g.,
pathogenesis of allergy and asthma. Primary T helper 2 cells are generated via in vitro culture under Th2 polarizing conditions using peripheral blood lymphocytes isolated from cord blood.	Assays for measuring calcium flux are well-known in the art and may be used or routinely modified to assess the ability of polypeptides of the	and agonists or antagonists of the invention) to mobilize calcium. For example, the	rLFK assay may be used to measure influx of calcium. Cells normally have very low concentrations of cytosolic calcium compared to much	higher extracellular calcium.  Extracellular factors can cause an influx of calcium, leading to activation of calcium	responsive signaling pathways and alterations in cell functions. Exemplary assays	modified to measure calcium flux by polypeptides of the
	Stimulation of Calcium Flux in pancreatic beta cells.					
	1275					
	HMAMI15					
	327					

seiboding antibuling antibodies	heart disease othersocie
ond sequence as attained of the	micant discast, aniciosolotosis,
and agomets of antagomets of	filiciovascular disease,
the invention) include assays	hypertension, stroke, and other
disclosed in: Satin LS, et al.,	diseases and disorders as
Endocrinology, 136(10):4589-	described in the
601 (1995);Mogami H, et al.,	"Cardiovascular Disorders"
 Endocrinology, 136(7):2960-6	section below), dyslipidemia,
(1995); Richardson SB, et al.,	endocrine disorders (as
Biochem J, 288 (Pt 3):847-51	described in the "Endocrine
(1992); and, Meats, JE, et al.,	Disorders" section below),
 Cell Calcium 1989 Nov-	neuropathy, vision impairment
Dec;10(8):535-41 (1989), the	(e.g., diabetic retinopathy and
contents of each of which is	blindness), ulcers and impaired
herein incorporated by	wound healing, and infection
reference in its entirety.	(e.g., infectious diseases and
Pancreatic cells that may be	disorders as described in the
used according to these assays	"Infectious Diseases" section
are publicly available (e.g.,	below, especially of the
through the ATCC) and/or	urinary tract and skin), carpal
may be routinely generated.	tunnel syndrome and
Exemplary pancreatic cells that	Dupuytren's contracture).
may be used according to these	An additional highly preferred
assays include HITT15 Cells.	indication is obesity and/or
HITT15 are an adherent	complications associated with
epithelial cell line established	obesity. Additional highly
from Syrian hamster islet cells	preferred indications include
transformed with SV40. These	weight loss or alternatively,
cells express glucagon,	weight gain. Aditional
somatostatin, and	highly preferred indications are
glucocorticoid receptors. The	complications associated with
cells secrete insulin, which is	insulin resistance.

stimulated by glucose and glucagon and suppressed by somatostatin or glucocorticoids. ATTC# CRL-1777 Refs: Lord and Ashcroft. Biochem. J. 219: 547-551; Santerre et al. Proc. Natl. Acad. Sci. USA 78: 4339-4343, 1981.		Assays for activation of transcription are well-known in the art and may be used and routinely modified to assess ability of polypeptides of the invention to inhibit or activate transcription. An example of such an assay follows: Cells were pretreated with SID supernatants or controls for 15-18 hours. SEAP activity was measured after 48 hours. LS174T is an epithelial colon adenocarcinoma cell line. Its tumourigenicity in nude mice make cell line LS174T a model for studies on the mechanism of synthesis and secretion of specific tumoral markers in colon cancer. See, Patan et al.,
	CD152 in Human T cells	Activation of Transcription
	1275	1275
	HMAMI15	HMAMI15
	327	327

				Circ Res, 89(8):732-39 (2001), the contents of which are herein incorporated by reference in its entirety.	
328	HMDAE65	1276	Production of IL-6	IL-6 FMAT. IL-6 is produced by T cells and has strong effects on B cells. IL-6 participates in IL-4 induced IgE production and increases IgA production (IgA plays a role in mucosal immunity). IL-6 induces cytotoxic T cells. Deregulated expression of IL-6 has been linked to autoimmune disease, plasmacytomas, myelomas, and chronic hyperproliferative diseases. Assays for immunomodulatory and differentiation factor proteins produced by a large variety of cells where the expression level is strongly regulated by cytokines, growth factors, and hormones are well known in the art and may be used or routinely modified to assess the ability of polypeptides of the invention (including antibodies and agonists or antagonists of the	A highly preferred embodiment of the invention includes a method for stimulating (e.g., increasing) IL-6 production. An alternative highly preferred embodiment of the invention includes a method for inhibiting (e.g., reducing) IL-6 production. A highly preferred indication is the stimulation or enhancement of mucosal immunity. Highly preferred indications include blood disorders (e.g., as described below under "Immune Activity", "Blood-Related Disorders", and/or "Cardiovascular Disorders"), and infection (e.g., as described below under "Infectious Disease"). Highly preferred indications include autoimmune diseases (e.g., rheumatoid arthritis, systemic lupus erythematosis, multiple sclerosis and/or as described
				invention) to mediate	below) and

		immunomodulation and	immunodeficiencies (e.g., as
		differentiation and modulate T	described below). Highly
		cell proliferation and function.	preferred indications also
		Exemplary assays that test for	include boosting a B cell-
		immunomodulatory proteins	mediated immune response
		evaluate the production of	and alternatively suppressing a
		cytokines, such as IL-6, and	B cell-mediated immune
		the stimulation and	response. Highly preferred
		upregulation of T cell	indications include
		proliferation and functional	inflammation and
		activities. Such assays that	inflammatory
	-	may be used or routinely	disorders.Additional highly
		modified to test	preferred indications include
		immunomodulatory and	asthma and allergy. Highly
		diffferentiation activity of	preferred indications include
		polypeptides of the invention	neoplastic diseases (e.g.,
		(including antibodies and	myeloma, plasmacytoma,
		agonists or antagonists of the	leukemia, lymphoma,
		invention) include assays	melanoma, and/or as described
		disclosed in Miraglia et al., J	below under
		Biomolecular Screening 4:193-	"Hyperproliferative
		204(1999); Rowland et al.,	Disorders"). Highly preferred
		"Lymphocytes: a practical	indications include neoplasms
		approach" Chapter 6:138-160	and cancers, such as, myeloma,
		(2000); and Verhasselt et al., J	plasmacytoma, leukemia,
		Immunol 158:2919-2925	lymphoma, melanoma, and
		(1997), the contents of each of	prostate, breast, lung, colon,
		which are herein incorporated	pancreatic, esophageal,
		by reference in its entirety.	stomach, brain, liver and
		Human dendritic cells that may	urinary cancer. Other preferred
		be used according to these	indications include benign

			assays may be isolated using	dysproliferative disorders and
			otherwise known in the art.	as, for example, hyperplasia,
			Human dendritic cells are	metaplasia, and/or dysplasia.
	_		antigen presenting cells in	Preferred indications include
			suspension culture, which,	anemia, pancytopenia,
			when activated by antigen	leukopenia, thrombocytopenia,
			and/or cytokines, initiate and	Hodgkin's disease, acute
			upregulate T cell proliferation	lymphocytic anemia (ALL),
			and functional activities.	multiple myeloma, Burkitt's
				lymphoma, arthritis, AIDS,
				granulomatous disease,
				inflammatory bowel disease,
				sepsis, neutropenia,
				neutrophilia, psoriasis,
				suppression of immune
				reactions to transplanted
				organs and tissues,
				hemophilia, hypercoagulation,
		-		diabetes mellitus, endocarditis,
				meningitis, and Lyme Disease.
				An additonal preferred
				indication is infection (e.g., an
	-			infectious disease as described
				below under "Infectious
				Disease").
HMDAM24	1277	Protection from	Caspase Apoptosis Rescue.	A highly preferred
		Endothelial Cell	Assays for caspase apoptosis	embodiment of the invention
		Apoptosis.	rescue are well known in the	includes a method for
			art and may be used or	stimulating endothelial cell
ļ			routinely modified to assess	growth. An alternative highly